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CANCER OF THE BREAST*

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AT THE New York Skin and Cancer Hospital (now the Tumor Clinic of the New York Post-Graduate Hospital) the teaching has always been in vogue that any breast cancer, with its accessible metastases, which is removable, is operable. In view of the seriousness of the disease, any reasonable attempt to save or relieve a patient is justified.

We have divided our cases into three main groups:

Group I.—Primarily Operable Cases: Under this heading are included all those cases without definite evidence of incurability. It is our belief that all cases which are operated upon in the hope of accomplishing a cure must be classed as primarily operable. The fact that the prognosis seems unfavorable in many should not change this attitude. In this sense, all cases with axillary involvement are operable but unfavorable, as indicated by published statistics, most of which report not more than about 20 per cent of five-year results. In the same way, if we study patients with ulcerated carcinoma of the breast as a group, we find the prognosis very grave. Of our 33 cases with ulceration only two survived the five-year period. Nevertheless, if the breast is movable and there is no evidence of internal metastases, the lesion must be classed as primarily operable even though the five-year results are poor.

Group II.—Operable for Palliation: This is a group of cases with evidence of incurability. Operation is performed for the relief of symptoms. Many of the patients are referred to us after unsuccessful radiation treatment or an incomplete operation performed elsewhere. Ulcerated lesions affecting the chest wall are included, as well as patients with inflammatory carcinoma which do not permit operation within normal tissue.

Group III.—Inoperable Cases: Classed as inoperable are only those cases with the local primary tumor involving the chest wall so extensively that

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complete removal is impossible, or with the axillary or supraclavicular nodes involved to such an extent that they cannot be extirpated. In addition to these, all cases with known distant metastases are rejected for operation. Occasionally, however, operation may be permissible in such cases for the relief of symptoms or for the removal of a foul, ulcerating lesion.

The present report is based upon a group of 278 consecutive cases operated upon during the ten-year period, 1924–1933 inclusive. The findings are supplemented by observations based upon personal experience with the disease. At our hospital the treatment of cancer of the breast has always been primarily surgical in the operable cases. Radiation treatment, either pre- or postoperative, was used routinely during a certain period covered by this paper, and is being used to-day in selected cases. The operations were performed by an attending staff and their resident assistants, 34 in number.

Among the applicants, 505 were clinically diagnosed as carcinoma, and may be classified as follows: (1) One hundred eleven, or 22 per cent, were considered inoperable. About one-half of them were neglected primary cases, which had received neither surgical nor roentgenotherapy, while the other half were patients with recurrences and metastases. (2) Three hundred ninety-four cases were classed as operable. Of these, 116, or 23 per cent, came for consultation only, leaving 278, or 55 per cent, which form the basis of the present report.

They are divided into: (a) Primarily operable, 253 in number, selected on the basis of the criteria of operability previously defined. (b) Cases for palliative surgery, 25 in number, or 9 per cent, including local recurrences, advanced, ulcerative tumors and inflammatory lesions presenting evidence of incurability.

Mode of Onset.—Patients with carcinoma of the breast usually complain of the accidental discovery of a painless lump as the first manifestation of trouble. Some are so unobservant, however, that their attention is not drawn to the breast until there is gross deformity, ulceration, pain, or bleeding, as indicated in Table I:

TABLE I

FIRST MANIFESTATION OF CANCER

	Tumor	Ulceration	Pain	Deformity	Bleeding	Discoloration	Cracked Nipple	Not Given	Total
No. of Cases.....	215	15	12	12	6	1	2	15	278
Per Cent.....	77.3	5.4	4.3	4.3	2.1	0.4	0.8	5.4	100

Largely as the result of the educational campaigns conducted by the American Society for the Control of Cancer, and other agencies, many patients seek medical advice on the first appearance of one of these symptoms. Unfortunately, however, a large number delay because of the dread of being told they have cancer, or because they consider the manifestation not of sufficient importance to consult a physician.

The statistics detailed in Table II indicate the unnecessary delay oc-

casioned by such an attitude. This delay permits the tumor to grow from one which may be curable to one which offers a less favorable prognosis.

TABLE II

LENGTH OF DELAY BETWEEN ONSET OF SYMPTOMS AND SURGICAL CONSULTATION

21 or	7.5%	Came within 1 month
20 or	7.2%	Came between 1 and 2 months
37 or	13.3%	Came between 2 and 4 months
24 or	8.6%	Came between 4 and 6 months
Only 102 *or*	36.6%	*Came within the first 6 months*
153 or	54.9%	Came within 1 year
40 or	14.4%	Came between 1 and 2 years
20 or	7.2%	Came between 2 and 3 years
22 or	7.9%	Came after 3 years
43 or	15.5%	Onset not stated
278 or	100.0%	

Experience has shown that early operations for carcinoma lead to far better results than those performed late in the disease, no matter how radically they are performed. When a patient presents herself with a lump in the breast, it is the physician's duty not to shoulder the responsibility alone but to refer her to a surgeon for opinion and establishment of a definite diagnosis. In a large percentage of cases, a clinical diagnosis of carcinoma is possible with reasonable certainty. In all doubtful cases, and this applies particularly to the early, favorable ones, a biopsy should be suggested.

Physical Signs of Cancer.—There are definite physical signs which aid in the diagnosis of carcinoma, such as hardness of the tumor, an ill-defined border, fixation, deformity, elevation of the breast, retraction of the nipple, puckering of the overlying skin, pigskin appearance, bleeding from the nipple or enlargement of axillary lymph nodes. When all of these signs are present, the case is an advanced one and the diagnosis is, of course, easy, with a correspondingly unfavorable prognosis. It is, therefore, important to make a diagnosis when only one or two of these signs are present. No matter how small the tumor, when it is hard, ill-defined, and there is the slightest retraction of the overlying skin, malignancy has to be strongly suspected. There may be no skin retraction visible on inspection, but on elevating the breast or approximating the skin over the site of the tumor, slight dimpling may appear and should arouse suspicion. Operations performed at this stage yield the best results. Transillumination is of relatively little value.

There are types of carcinoma which do not present the physical signs mentioned above. The tumor may be smooth and freely movable and, clinically, indistinguishable from a benign growth. Because of this fact, no physician can afford to say to a patient over 30 years of age, "This lump is a harmless little gland, don't worry about it." Procrastination may cause that patient to lose her life. Whether a positive clinical diagnosis is possible or not, every breast tumor in a patient over 30 years of age should be excised and a definite diagnosis established.

Incidence of Diagnostic Signs.—Physical examination of the 278 cases herewith reported revealed the following findings of diagnostic importance:

(1) *Definite Tumor.*—These were found in 96 per cent of the cases, while in 4 per cent there was diffuse infiltration. In 20 per cent there were no physical signs except a small, hard, ill-defined, more or less movable nodule. In spite of that, 14 per cent of this group showed axillary lymph node involvement.

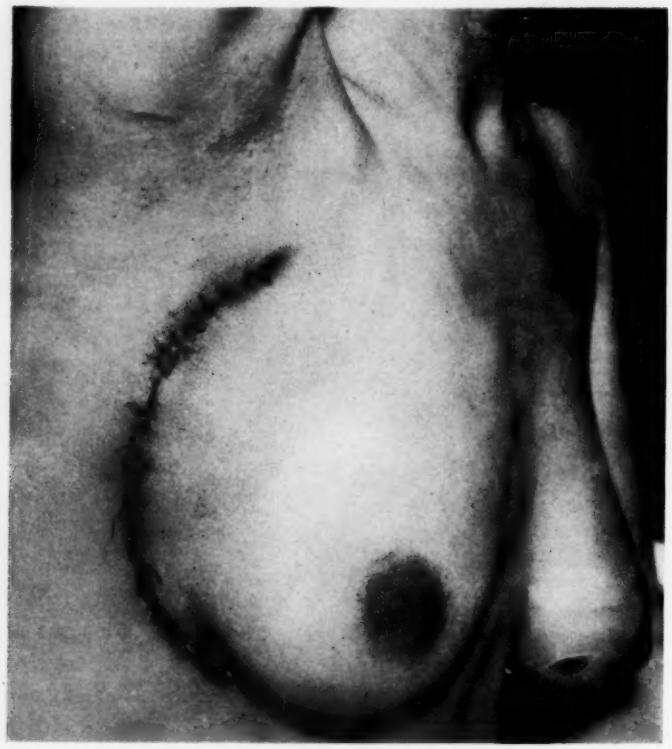

FIG. 1.—Nondisfiguring incision along the margin of the breast for excision of tumors.

(2) *Location of the Tumor.*—The site of the tumor was mentioned in 226 cases (Table III).

TABLE III

LOCATION OF TUMOR

	Right	Left	Total	Per Cent
Upper outer quadrant	56	54	110	48.6
Upper inner quadrant	22	14	36	15.9
Lower outer quadrant	17	18	35	15.5
Lower inner quadrant	7	8	15	6.6
Central	12	18	30	13.3
Totals	114	112	226	100.

Table III shows that in 110 cases, or 48.6 per cent, the tumor was situated in the upper outer quadrant. This location is, therefore, of diagnostic importance. In this connection it may be emphasized that localized chronic mastitis, also, nearly always affects these same regions. The differential

diagnosis between the two conditions is, therefore, important and, at times, so difficult that only a biopsy will clear it up. This may be undertaken without resultant disfigurement, by a semilunar incision along the outer and inferior margin of the breast, separating it from the chest wall and everting it. The entire involved area is then excised in a wedge-shaped manner, with the apex toward the nipple.

(3) *Pain.*—This was present as the first symptom in only 12 cases, or 4.3 per cent. It was present with the tumor in 46 cases, or 16.5 per cent. Pain usually means advanced disease, an infiltrating carcinoma, or association of carcinoma with chronic cystic mastitis.

(4) *Adherent Skin.*—This was mentioned in 158 cases, or 57 per cent. It is of special importance in the early cases, in which other signs are lacking, and may be the only real clue to the true diagnosis. When there is extensive deformity of the breast, pigskin appearance or ulceration, these signs naturally overshadow it.

(5) *Deformity.*—This was noted in about 25 per cent of the cases. No definite statistics are available because this condition is frequently combined with elevation of the breast or retraction of the nipple which, in themselves, produce deformity. Sometimes the breast is markedly shrunken by a gradual destructive process. In other cases it is enlarged by the presence of a massive tumor or with an inflammatory carcinoma.

(6) *Retraction of the Nipple.*—This was noted in 92 cases, or 33.1 per cent. This sign apparently indicated advanced disease, as in 88 per cent of the cases so affected there was axillary lymph node involvement.

(7) *Pigskin Appearance.*—This indicates a very malignant tumor with blocking of the ducts and edema. It is one of the chief signs in diffuse duct carcinoma, as well as in inflammatory carcinoma. It was reported in 27 instances, or 13.3 per cent.

(8) *Ulceration.*—This is usually considered a sign of advanced disease, and consequently operation is frequently withheld. In our group, there were 33 patients with ulceration. In eight, or 24.2 per cent, the axillary lymph nodes were found not to be involved. Only two cases survived the five-year period. Nevertheless, we feel that, although ulceration is usually indicative of a grave prognosis, the lesion may be operable, and may be completely extirpated together with the axillary metastases. We have, therefore, included all but four of our cases with ulceration in which no internal metastases could be demonstrated, and in which the lesions were removable, with our primary operable cases. The other four are included in our list of cases in which a palliative operation only was performed. Resection of a part of the chest wall is at times necessary. Electrosurgery finds its greatest application in this group of cases.

(9) *Bleeding Nipple.*—This was encountered in six cases; in all instances it was the first sign of malignant involvement. *The significance of bleeding and other discharges from the nipple* is a subject which requires careful attention.

Clinically, the problem is often quite difficult. If, in the presence of bleeding or other discharge, a nodule is palpable, and especially if pressure on this nodule increases the discharge, its removal and subsequent examination will clear up the diagnosis. These tumors, with their papillary ingrowths, are usually small, and are situated under or close to the border of the areola. They may be removed by a non-disfiguring incision along the margin of the areola, as shown in Figure 2.

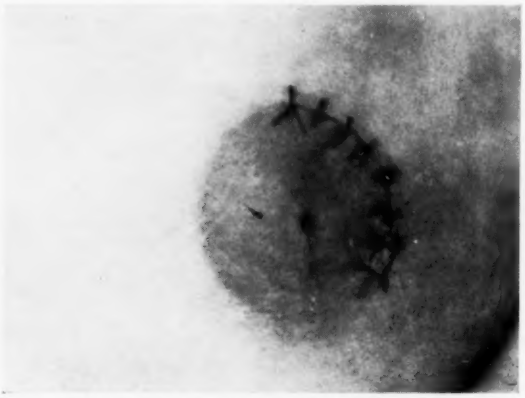

FIG. 2.—Nondisfiguring incision along the margin of the areola for the excision of small tumors under the areola or from the adjoining breast tissue.

Frequently, however, no nodule is palpable and there is nothing to guide one in the selection of the site for the incision. Clinical experience here is of great value. Cases with serous and other discharges may be regarded as probably benign and treatment instituted to relieve them. They should, however, be kept under observation. Knowing that a large percentage of patients with bleeding nipples have carcinoma, its clinical significance should be stressed. The condition should be discussed with the patient and her family. If the bleeding persists it is important that some operative procedure be employed to determine the source of the bleeding. A simple ablation may be indicated.

(10) *Axillary Lymph Node Involvement.*—Axillary lymph nodes were palpable in 160 cases. In eight, or 5 per cent, they were later shown not to be malignant. Axillary lymph nodes were not palpable in 76 cases. Cancer was found in seven of these, or 9.2 per cent. Their presence was not mentioned in 42 cases.

Relation of Size of Primary Tumor to Axillary Metastases.—In the group of cases herewith presented, the percentage of axillary metastases is in direct relation to the size of the tumor (Table IV).

Table IV indicates that a small tumor is probably an early tumor. There is progressive axillary involvement with increasing size of the tumor. Such increase may mean that we are dealing with an old tumor, or one of rapid growth and high malignancy.

TABLE IV

RELATION OF SIZE OF TUMOR TO AXILLARY METASTASES

Size of Tumor	½ cm.	1 cm.	2 cm.	3 cm.	4 cm.	5 cm.	6 cm.	7 cm.	8 cm.	9 cm.	10 cm.	Larger Than 10 cm.	Size Not Mention	Totaled
No. of Cases	5	12	23	50	35	24	18	11	7	5	4	18	66	278
No. of Involved Axillary Modes	1	3	7	30	24	20	17	9	6	5	4	18	52	185
Per Cent	20	25	30.4	60	68.5	83.3	94.4	81.8	85.6	100	100	100	78.7	66.5

Principles of the Radical Operation.—The operation employed by us bears the names of Halsted and Willy Meyer, in honor of the two men who have done most to standardize the procedure. As is well known, the essential difference between the Halsted and Willy Meyer procedure is that the former began his dissection at the sternum and worked toward the axilla, while the latter started at the axilla and dissected toward the median line in the hope of avoiding dissemination of cancer cells by manipulation of the tumor during operation.

Technic of the Operation.—We follow the Willy Meyer procedure, with some minor changes which have proved of value. The landmarks of the skin incision are the insertion of the pectoralis major muscle at the humerus, the junction of the middle and outer third of a line drawn from the clavicle to the free axillary border of the pectoralis major, and a point midway between the lower margin of the breast and the umbilicus. The variable landmarks are at the breast. The incision here surrounds the breast and depends upon the location and size of the tumor. Practically the entire skin of the breast must be removed, but this is varied slightly depending upon which quadrant of the breast is involved. All the landmarks are joined by the skin incision, which constitutes the first step. The important point is not to worry about the subsequent closure of the wound, but rather to be sure to stay well away from the tumor in order to avoid the all too frequent recurrences in the skin.

The next step is to carry the skin incision only into the superficial fat. The skin flaps are undermined and the dissection carried to the deep landmarks, which are the cephalic vein above and outward, the clavicle above, the sternum mesially and the rectus sheath below. Laterally, it extends to the free border of the latissimus dorsi muscle with its tendinous attachment to the humerus. When these landmarks are reached the entire incision is deepened to the fascia and muscles.

The actual dissection begins just above the cephalic vein on the deltoid muscle and is carried downward across the vein, taking away all fat and fascial covering of muscles and vessels. It cleans out the infraclavicular fossa above and exposes the insertion of the pectoralis major muscle at the humerus. The fibers of the pectoralis major muscle are separated from those of the deltoid. The cephalic vein marks this division. Then the entire muscular and tendinous attachment of the pectoralis major muscle is divided close

to the humerus. This preliminary step naturally means the later removal of the entire muscle including the clavicular portion. The dissection is carried over the coracobrachialis muscle.

The pectoralis minor muscle is readily exposed as it crosses the axillary vein and inserts into the coracoid process. The muscle is divided at the coracoid process, which exposes the entire axilla for careful dissection. In most cases, it is simpler to divide the broad attachment of the clavicular portion of the pectoralis major muscle at this time, before starting any dissection of the axilla, as this step immediately exposes the deep fascia covering the axillary contents, especially the axillary vein as it dips behind the clavicle which marks the uppermost portion of the axillary dissection.

A sharp scalpel is the best means of performing a thorough axillary dissection. This will remove all fat and fascia, exposing bare muscle, which will allow removal of the sheath of the axillary vein, to which are attached lymph nodes and lymph vessels. Injury to the junction of the cephalic with the axillary vein should be avoided. The only large vessels encountered, which must be divided, are the anterior thoracic artery and vein. Various other smaller vessels must be clamped and divided, the veins all being clamped within the sheath. The large nerves lying above the artery and vein should not be unnecessarily exposed. All veins entering the axillary vein from *below* can be immediately divided, the only one to be saved being the subscapular vein, which enters the axillary vein from *behind* in the outer portion of the axilla.

With the division of the deep fascia and axillary dissection the chest wall is exposed at the first rib. The highest portion of the subscapular space, way up behind the vessels, can be cleaned out by wiping it out with a gauze sponge. This is the only time that gauze dissection is employed. The long thoracic nerve of Bell, supplying the serratus magnus muscle, should be preserved. The subscapular artery and vein and nerve should also be preserved, unless they are included within a mass of involved malignant nodes, when they must be sacrificed for the sake of thoroughness.

Dissection is now carried across the chest wall from the latissimus dorsi muscle mesially, gently lifting the breast, pectoral muscles and axillary contents so that the serratus fibers may be freed of their fascia and the fibers of origin of the pectoralis minor muscle divided. The perforating branches of the internal mammary artery close to the sternum are divided and ligated with a few other branches of the intercostal vessels. Sometimes the upper rectus sheath is also removed, which leaves only the muscular fibers of origin of the pectoralis major muscle at the sternum to be divided. Thus the entire cancer field is removed *en bloc*. The high frequency current is employed for hemostasis of all smaller vessels.

A stab wound is made through the lateral flap, just anterior to the latissimus dorsi muscle, and two split-rubber tubes inserted into the axilla.

In case suture without undue tension is possible, the wound is completely closed with interrupted silk sutures. All air and fluid is expressed

from under the flaps, permitting close apposition of the skin to the chest wall. A pressure dressing is applied over the axilla.

The arm is put up in abduction and is kept that way. It is most important to do this in order to obtain early function of the arm. The first dressing is undertaken from the fifth to the seventh day, depending upon circumstances, chiefly amount of discharge, odor, or discomfort. The drainage tubes are removed at this time.

Subsequent dressings are also applied with the arm in abduction. The patient is allowed out of bed as soon as she feels like it and her general condition permits. Function of the arm is encouraged, and complete elevation is usually possible by the time the patient is discharged.

In case closure of the wound is not possible, a Thiersch skin graft from the thigh is done immediately. The graft is covered with silver foil and vaseline gauze. The dressing is not disturbed for seven days. Usually, the grafts take in their entirety.

Biopsies.—The question of biopsies requires special consideration. It is probably conceded by nearly all surgeons, that a biopsy, which consists of excision of the entire tumor with a margin of normal breast tissue, is without danger. In view of the fact that the clinical diagnosis of carcinoma is often doubtful, especially in the early cases, biopsy becomes a necessity. We have gone a step further, and in a communication,[3] in 1932, advocated excision of the entire tumor, not only for the purpose of establishing a diagnosis, but with the aim of avoiding manipulation of the growth during operation. We have always felt that some of the distant metastases to which patients finally succumb, are due to rough handling of the breast. When one considers the tendency of cancer to spread in all directions by direct extension along tissue spaces, through lymphatic channels to lymph nodes, or directly into the blood stream, it is conceivable that pressure upon the tumor itself, or upon some of the tumor emboli (Figs. 3. 4. and 5) in vessels, may propel them onward. When in addition to that, one considers that only those cancer cells which pass to the axillary lymph nodes are accessible, while those which travel along the perforating branches of the internal mammary vessels cannot be reached, the importance of trying to confine the tumor cells to the breast becomes apparent. From the moment a patient places herself under a surgeon's care he is responsible for her. Frequent or rough handling of the breast should be avoided. This applies to the preoperative period as well as to the operation itself. It is unavoidable for the assistant to pull or press on the breast during the operation. By a preliminary excision of the tumor, with either a scalpel or preferably an electrosurgical knife, this danger may be avoided.

In planning a biopsy, the patient should be prepared for a radical operaton. An incision, adequate for good exposure, is made, and the entire lesion is then excised with a good margin of normal breast tissue and fat. In case the growth is adherent to the skin, the involved portion of the latter

is also removed. Care is taken not to press upon or handle the tumor other than is absolutely necessary. In case of a favorable pathologic report, the edges of the breast tissue are approximated with a few plain catgut sutures, a split-tube drain is inserted if indicated, and the skin closed with inter-

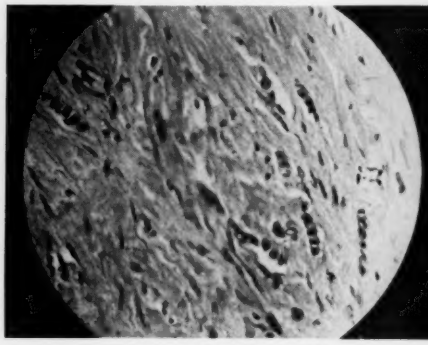

FIG. 3.—Direct extension of carcinoma cells in tissue lymph sinuses.

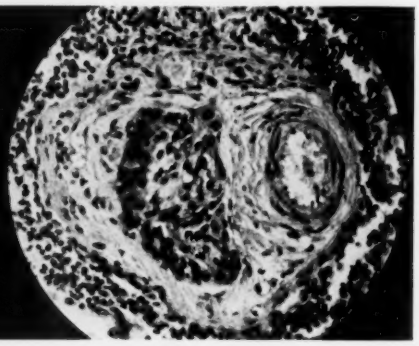

FIG. 4.—Carcinoma metastasis in a vein of a lymph node.

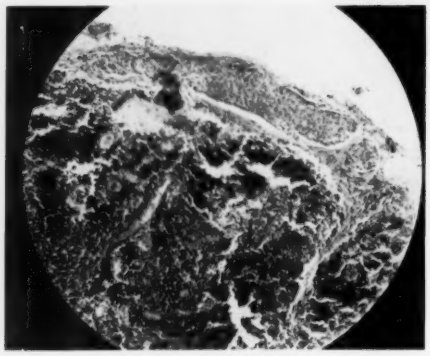

FIG. 5.—Carcinoma metastasis in the lateral sinus of a lymph node.

rupted silk. Should the tumor prove to be malignant, a small antiseptic tampon is inserted into the wound, the skin is closed with a few sutures, and the radical operation immediately undertaken.

Postoperative Results.—Variations in postoperative results are frequently observed in spite of the constancy of operative method and individual skill. They probably depend, to a large degree, upon differences in malignancy as well as on the extent of the disease. It may well be assumed that the majority of the patients who succumb within two years after operation, have tumors of a high degree of malignancy. It is these same cases which may have deep-seated, unrecognizable internal metastases at the time of operation, even though the axilla is negative. It is our belief that the prognosis depends on three factors: Early diagnosis; the thoroughness of the radical operation; and the degree of malignancy of the tumor. The observation that certain

tumors, classified histologically, give a higher percentage of "cures" than other groups is indicated in Table X. It is also known that certain patients have clinically favorable tumors regardless of the histology (Figs. 6 and 7 A and B). Having a large number of such favorable cases in any reported group will naturally improve the statistics.

FIG. 6.—Adenocarcinoma Grade 2. "A favorable tumor." Radical operation 14 years after onset. Axillary nodes not involved.

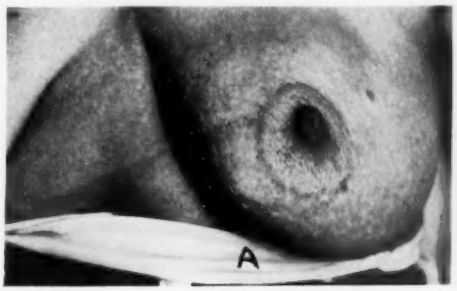

FIG. 7.—(A) Typical duct carcinoma with retraction of nipple and edema of skin, of three year's duration. Axilla involved. (B) Result eight years after operation. No signs of metastases. "A favorable tumor."

In order to permit comparison of our statistics with those of others, we have included all cases operated upon that offered a chance of cure, according to the criteria for operation enumerated above (Table V).

TABLE V

RESULTS IN ALL PRIMARILY OPERABLE CASES

Operations in cases classed as primarily operable	253
Operability	91.0%
Five-year arrests	85 or 33.5%
Ten-year arrests (of 97 cases operated upon 10 years before)	21 or 21.7%
Axillary nodes not involved	92 or 36.3%
Five-year arrests	51 or 55.6%
Ten-year arrests (of 36 cases operated upon 10 years before)	13 or 36.1%
Axillary nodes involved	161 or 63.7%
Five-year arrests	34 or 21.2%
Ten-year arrests	8 or 13.1%
Follow-up obtained on (of the total of 278 cases)	249 or 89.5%

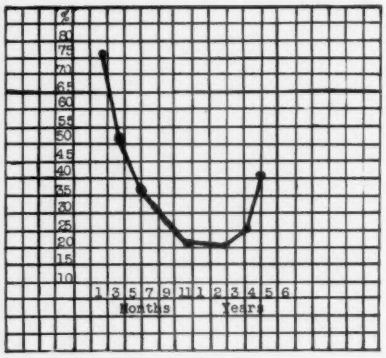

CHART 1.—Illustrating the percentage of five-year arrest cases in relation to operative delay: There is a gradual reduction in five-year arrests in cases in which operation was delayed from one month up to two years. After that, there is a definite increase in recoveries.

The probable explanation is that the more malignant cases die during the first two years after recognition of the tumor. Those who survive probably represent so-called favorable tumors from a malignancy standpoint. Either the cells in themselves, are less malignant or the resistance of the host is greater than usual.

Prognostic Significance of Delay.—Table VI shows the relation between delayed operation and five-year arrest. This study is based upon 235 cases in which definite information was obtainable. The 43 cases in which no positive data were available have been excluded (Chart I).

Prognostic Significance of Tumor Size.—All tumors excised at our clinic are measured and studied in relation to the other portions of the breast. The statistics in Table VII show, as one may expect, that the chances of five-year arrest are better with smaller tumors, and indicates the importance of early diagnosis and operation. The smaller the tumor, the younger it apparently is, and the better the operative results.

TABLE VI

FIVE-YEAR RESULTS AS INFLUENCED BY DELAY IN OPERATING

	Operated Within	Between					3 Yrs.
Operated	1 Mo.	1–2 Mos.	2–6 Mos.	6 Mos.–1 Yr.	1–2 Yrs.	2–3 Yrs.	(or longer)
No. of Cases	21	20	61	51	40	20	22
Five-year Arrest	16	10	21	12	8	5	9
Per Cent	76	50	34	23	20	25	40.9

Tables VI and VII present statistical evidence of the importance of operating upon patients soon after discovery of the growth and while the tumor is still small. A five-year operative recovery, of about 75 per cent, in these early cases may confidently be expected.

TABLE VII

RELATION BETWEEN SIZE OF TUMOR AND FIVE-YEAR ARREST

												Over	Not
	½	1	2	3	4	5	6	7	8	9	10	10	Men-
Size	cm.	cm.	cm.	cm.	cm.	cm.	cm.	cm.	cm.	cm.	cm.	cm.	tioned
No. of Cases	5	12	23	50	35	24	18	11	7	5	4	18	66
Alive Five Yrs.	2	6	21	14	10	6	1	2	1	1	0	3	23
No. of Cases		40			127					45			66
Five-yr. Arrest		29			31					7			23
Per Cent		72.5			24.4					15.5			32

Roentgenotherapy.—Opinions still differ widely as to the advantages of roentgenotherapy, either before operation or after the radical operation. Largely influenced by our observation that local recurrences are rare, and that the patients who die of carcinoma after a radical operation succumb

to deep-seated regional or distant metastases, we are, at present, not using postoperative radiation as a routine, but only in cases which had axillary involvement and otherwise appear as unfavorable. Postoperative radiation, in order to be effective, would have to be administered over the whole body, but this is not feasible. To concentrate on the operative scar, axilla and mediastinum is not going to affect distant metastases though it may be valuable in destroying tumor cells in regions adjacent to the growth. We occasionally use preoperative radiation for carcinoma with a bad prognosis, especially the inflammatory type. Its value is questionable.

During a part of the period covered in the present communication, postoperative radiation was used routinely. Of the 278 cases reported, 101 had radiation in some form, four preoperatively, four pre- and postoperatively, and 93 postoperatively alone. Whereas, of the total group of 278 cases there was five-year arrest in 32.3 per cent of cases, in the group of 101 cases treated with radiation in addition to operation, there was a five-year arrest of 38.7 per cent.

The cases were not selected, and on the basis of these statistics, it appears that there may be merit in radiation following a carefully performed radical operation.

Comparative Statistics of Cases Treated Surgically.—A comparison of our statistics with those of other institutions is presented in Table VIII.

TABLE VIII

COMPARATIVE STATISTICS—FIVE-YEAR RESULTS

	Total Cases Per Cent	Without Axillary Involvement Per Cent	With Axillary Involvement Per Cent
Willy Meyer[8] (German Hosp.)	30		
Mathews[7] (St. Luke's Hosp.)	37.8		
Sistrunk and McCarthy[9] (Mayo Clinic)	36.7	63.9	18.9
Eggers[3] (Lenox Hill Hosp.)	43.8	65.4	33.3
Harrington[4] (Mayo Clinic)		71.2	26.3
Klingenstein[6] (Mt. Sinai Hosp.)	23	40	17
White[10] (Roosevelt Hosp.) 1927	36	70	19
1937	27	58	12
Eggers, de Cholnoky and Jessup (N. Y. Skin and Cancer Hosp.)	33.5	55.6	21.2

Table VIII indicates that the more recent communications present no improvement in results over the older ones. Willy Meyer's[8] report, in 1905, which includes all his cases since he proposed the radical operation in 1894, and presents 30 per cent five-year results obtained in unselected cases, is as good as those reported from most clinics to-day, even with the addition of postoperative radiation. White's[10] communications, in 1927 and 1937, are interesting as showing that in spite of becoming more radical in his operative procedure and adding postoperative radiation, his statistics, in 1937, are well below those of 1927. As he himself states, this may be due to more accurate pathologic reports and a better follow-up. Perhaps uniform criteria of operability will aid in comparing statistics.

We would like, at this point, to refer to an article on cancer by one of

us,[3] in which a group of 80 consecutive, personal cases of breast cancer is reported. They represented all types of cancer and all degrees of severity. No radiation was employed. Emphasis was placed on wide excision of the tumor, thorough undermining of the skin and careful dissection. The total five-year arrest of the disease occurred in 43.8 per cent. The most striking result, however, was obtained in cases with axillary involvement, showing five-year arrest of the disease in 33.3 per cent of the cases, which is considerably higher than the recoveries reported from most clinics. We have attributed these results to careful surgery in the advanced cases. A comparison of the statistics of this group and the one reported herewith is presented in Table IX.

TABLE IX

COMPARATIVE STATISTICS

	Eggers. (Lenox Hill Hosp.)	Eggers, de Cholnoky and Jessup. (N. Y. Skin and Cancer Hospital)
Total cases	80	253
Operability	94.5%	91.0%
Five-year arrests	43.8%	33.5%
Ten-year arrests	15.0%	21.7%
Axillary nodes not involved	32.5%	36.3%
Five-year arrests	65.4%	55.6%
Ten-year arrests	18.3%	36.1%
Axillary nodes involved	67.5%	63.7%
Five-year arrests	33.3%	21.2%
Ten-year arrests	10.0%	13.1%
Follow-up	95.0%	89.5%

It raises the question—what is responsible for such marked differences in two groups in which practically the same criteria of operability and similar radical technic was employed? It appears to us that in addition to variability in degree of malignancy we may attribute them to two factors: (1) Poorer material in our clinic cases, which is about the least favorable imaginable. (2) Cases operated upon by one operator, with a well-developed technic, are likely to give better results than a group operated upon by 34 different surgeons, some of whom are just learning the technic.

Bilateral Cancer of the Breast.—It is known that about 5 per cent of patients with breast cancer develop a tumor in the opposite breast, either simultaneously or sometimes months or years after the first breast was removed.

It is interesting to speculate on whether the tumor is a metastasis from the primary growth or whether it is an independent lesion. Sometimes one, then the other theory, seems to apply. Occasionally the second involvement appears to be a direct extension across the median line.

In case the appearance of a tumor in the second breast coincides with the presence of deep-seated metastases, or if it shows the same pathologic structure, or if it appears simultaneously with, or soon after, the first growth, one may assume that metastatic involvement is the most likely explanation. On the other hand, if the second breast becomes involved only after several years, if there is no evidence of other metastases, and the patient remains

well for years after the second operation, one may reasonably assume that the tumor was an independent lesion.

It is our belief that, in the absence of proved metastases, a radical operation should be performed for malignant involvement of the second breast.

FIG. 8.—Radical operation for bilateral carcinoma. Note good functional result.

The same criteria of operability which apply in unilateral, should be applied in bilateral cases. All such cases should, therefore, be included in statistics of primarily operable lesions. The functional result after bilateral radical operation is good (Fig 8).

There were nine cases in our group, of which five, or 55.5 per cent lived beyond the five-year period, from the time of the first operation. One patient is living to-day, 12 years after the first operation. The axilla on one side was involved. One case died, six years after a bilateral operation, while two patients were lost from follow-up, six years after a bilateral operation performed the same year. Both were well when last seen and, in view of the fact that both had a cystadenocarcinoma, which is rated as a low grade tumor, it is possible that they are still alive. The other cases lived five, four and one-half, four, two and one year, and usually died soon after the second operation.

Supraclavicular Lymph Node Involvement.—This condition is rarely pres-

ent at the time primarily operable cases come under observation and, therefore, does not play a rôle in determining operability. During the ten-year period covered by this present report, 21 cases with supraclavicular enlargement were observed. Six cases may be eliminated because they were old, advanced, recurrent cases in which the primary operation had been performed elsewhere. One patient was not operated upon. This leaves 14 cases for consideration. In only one were the nodes present and removed at the time of the radical breast operation. It was evidently a bad case, because death resulted three months later. Two cases were operated upon within a month after the first radical operation, and the nodes showed only an hyperplasia. In the other 12 cases, the operation was performed in from several months to four years after the radical operation. All showed carcinomatous involvement.

Enlarged nodes were palpable in	15 cases
Not operated upon	1 case
Operated upon	14 cases
Involved with carcinoma	12 cases
Hyperplasia	2 cases
Follow-up on	10 cases
No follow-up on	2 cases

Of the patients who were operated upon for supraclavicular involvement the following follow-up was obtained:

Dead Within	1 yr.	2 yrs.	3 yrs.	3½ yrs.	4 yrs.
No. of Cases	5	2	1	1	1

No case survived the five-year period, and it is questionable whether the operation is of any real value. When involved, there are usually other deep-seated metastases in the mediastinum. However, in view of the almost negligible mortality attending this operation, it is justified when a patient shows isolated supraclavicular nodes with no definite evidence of distant metastases. The nodes may sometimes be controlled for a time with irradiation.

Local Recurrences.—By local recurrences, we understand secondary growths, appearing some time after the radical operation, within the field of operation. This means in the skin along the line of incision, in the subcutaneous tissue, in muscle remnants or in the axilla. It is our feeling that the surgeon is responsible for such local recurrences, in that they indicate that not sufficient skin was removed or that the deep dissection was not adequate.

Secondary growths appearing in tissues adjacent to the field of operation, such as the ribs, cartilages, intercostal tissues, anterior mediastinal and supraclavicular lymph nodes are not classed as recurrences but as regional metastases. No attempt is made during the radical operation to remove any of these tissues, and the surgeon is, therefore, not responsible for the appearance of metastases in them.

With this clear understanding, we report local recurrences in 17 cases, or 6.7 per cent, in the 253 primarily operable cases, in which the radical operation was performed by our own staff. The percentage of local recur-

rences is really an index of the efficacy of the operative procedure. With the statistics reported by us, which include all types of cases, favorable as well as unfavorable, we believe that local cure may confidently be expected in all breast cancers in which the growth is limited to the breast and the axilla. Those patients who subsequently die, rarely succumb to a recurrence of the growth locally, but to internal metastases. When one is dealing with a tumor fixed to the chest wall, an ulcerated growth, or an inflammatory carcinoma, local recurrence may be expected. The treatment of local recurrences depends upon their nature. If suitable, excision with the scalpel or electrosurgical knife may be undertaken, with or without resection of a portion of the chest wall. In other cases, palliative roentgenotherapy is indicated.

Edema of the Arm.—Chronic lymphedema of the arm is an unsightly and quite a disabling complication, which may be due to different causes. Judging from the fact that ligation of the axillary vein in several cases has not resulted in edema we believe it to be usually due to lymphatic blocking and only rarely to a phlebitis. A slight edema may be transitory or persistent, and is probably due to complete extirpation of the axillary lymph nodes with consequent interruption of lymph channels. We believe that chronic edema may be due to several factors: (1) Tight bandaging of the arm in a cramped position. (2) Unduly prolonged immobilization of the arm. (3) Postoperative roentgenotherapy. (4) Acute lymphangitis. (5) Phlebitis.

In our experience, it is an uncommon complication. We attribute this to the avoidance of the factors just mentioned. By putting the arm up in abduction and allowing free elbow motion from the start, good circulation in the arm is possible. Early elevation of the arm is encouraged and patients are taught exercises. They usually have a good range of motion at the time of discharge.

Although it cannot be proved, we have the definite clinical impression that early postoperative radiation favors the development of chronic edema, probably due to blocking of lymphatics by the formation of connective tissue before collateral lymphatic circulation has developed. At times, one sees acute edema developing several weeks after a perfectly normal convalescence. It is associated with redness and local heat, and corresponds to the clinical picture of acute lymphangitis. There is no other evidence of infection, and the condition subsides with elevation of the arm, rest, wet dressing, and ice bags.

When a chronic edema is definitely established it is most resistant to treatment. A daily period of elevation of the arm on several pillows, with the patient reclining, is of value. An elastic bandage applied lightly during the night will also aid in relieving the feeling of weight and tension.

Table X shows a pathologic classification which includes some terms that were in vogue 15 years ago, which have since been discarded by many pathologists—scirrhus and medullary being now employed as qualifying the general, broader designation of adenocarcinoma.

While histologic grading has been applied to these 278 cases, the re-

sults have not been tabulated here, for it has seemed to us that even with the most careful study of sections the conclusions, if offered to the clinician, are often misleading and that the most important feature in the study of breast tumors is the question of whether the growth is malignant or not.

TABLE X

PATHOLOGIC CLASSIFICATION

		Per Cent	Five-year Arrest	Per Cent
Scirrhus carcinoma	151	54.3	46	30.4
Medullary carcinoma	57	20.5	16	28.1
Adenocarcinoma	43	15.4	16	37.1
Paget's disease	5	1.8	3	60.0
Cystadenocarcinoma	4	1.4	2	50.0
Mucoid carcinoma	1	0.3	1	
Sarcoma	1	0.3	1	100.0
Basal cell carcinoma	1	0.3	1	
Unclassified carcinoma	15	5.4	6	40.0
Totals	278	100.0	92	32.2

If malignant, the treatment will be the same whether grade 1 or grade 3, and every patient is entitled to the standard radical operation where cancer is diagnosed.

Suggestions for Improving Results.—With the most favorable cases of cancer, those with a small movable tumor and no axillary lymph node involvement, the highest number of five-year results may reach 75 per cent, but it usually varies between 60 and 70 per cent. In the remaining 30 or 40 per cent of cases, death ensues some time within the five-year period, a large percentage dying within two years after operation. These patients rarely succumb to local recurrence, but die of internal metastases. We must assume, therefore, that even in this favorable group, cancer cells have spread from the local primary tumor into the body before or during the operation. The length of life of these patients depends upon the degree of malignancy of the tumor and upon the importance of the secondarily involved organs.

In patients with axillary involvement, ulceration, or bilateral cancer, the results are infinitely worse. The reports from large centers indicate that usually only about 20 per cent survive the five-year period, and frequently less.

Surgeons are alert to the need for salvaging a larger percentage of cases than is done at present. The following suggestions are offered in the hope of improving results:

(1) *Early Cases; Without Axillary Lymph Node Involvement.*—Many of the so-called early tumors must have been present longer than suspected, as indicated by the subsequent appearance of internal metastases. The question of earlier diagnosis and operation has to be approached from two points of view: (A) Education of the public to consult their physician regarding any breast symptoms, especially if a lump be present in the breast. (B) Continued education of the physician that any tumor of the breast should be considered a serious finding calling for immediate investigation. Early surgical

consultation is indicated and one should never hesitate to have a biopsy performed in order to reach a positive diagnosis. Other important factors to bear in mind are: (C) Avoid rough handling of the breast during examination. (D) Excise all breast tumors, especially in patients over 30 years of age, even if no definite signs of malignancy are present. (E) Practice wide preliminary excision of the tumor in contemplated radical operations, in order to prevent the spread of malignant cells by manipulation during operation. (F) Follow the old teaching "a small cancer, an extensive operation." Therefore, perform a radical, painstaking operation in all cases.

(2) *Advanced Cases.*—Those with gross axillary involvement, ulceration or bilateral breast cancer, but considered primarily operable. To be able to improve results in this group of cases, is a challenge to surgeons. It is our conviction that with careful handling of the breast; preliminary excision of the growth; thorough undermining of the skin; and the most meticulous clean dissection, good results may be expected in a fair percentage of cases. When comparing our five-year results in private cases with lymph node involvement with those published in reports from the larger centers, we feel that our contention for radical surgery has been justified. It is in this group of cases that local postoperative radiation may be of value.

SUMMARY

An analysis of 505 cases of breast cancer is presented from the Skin and Cancer Unit of the New York Post-Graduate Hospital. Being known as an institution devoted to the treatment of cancer, many patients came for consultation only, while others applied for relief from inoperable lesions.

One hundred eleven, or 22 per cent, had metastases which were internal or were irremovable and, therefore, inoperable. Three hundred ninety-four were considered operable. Of these 116, or 23 per cent, came for consultation only, leaving 278, or 55 per cent, which form the basis of this report. They are divided into two main groups:

Group I.—Primarily Operable Cases (253 in number): Definite criteria for operability are presented. They include all cases without demonstrable distant metastases, in which the entire breast, with its accessible lymph node metastases, can be removed. Cases with ulceration, supraclavicular involvement, and bilateral breast cancer are included.

Group II.—Cases for Palliative Surgery: Our group is composed of 25, or 9 per cent, of the cases, including local recurrences, advanced ulcerated tumors, and inflammatory carcinomata presenting evidences of incurability.

The prognostic significance of delay; size of tumor; axillary involvement; and subsequent prognosis is presented on the basis of five- and ten-year results.

The routine radical operation for primarily operable cases is described.

Preliminary excision of the tumor is advised in radical operations to avoid manipulation of the growth and the spread of cancer cells during operation.

By the two tests at our disposal for judging the efficacy of the radical operation for cancer of the breast—longevity and local recurrence—we may conclude that a carefully performed operation is successful in curing the disease locally.

A defeatist attitude and a timid approach to the subject spell failure.

Complications and sequelae are presented under the different headings of bilateral involvement; supraclavicular involvement; the significance of bleeding from the nipple and other discharges; ulcerated breast carcinoma; local recurrence; and chronic edema of the arm.

Mention is made of the value of radiation treatment.

A pathologic classification is submitted with five-year results in each group.

Suggestions for improving results are discussed.

Five-year arrests were obtained in cases without lymph node involvement in 55.6 per cent; with lymph node involvement in 21.2 per cent. Ten-year arrests were obtained in cases without lymph node involvement in 36.1 per cent, with lymph node involvement in 13.1 per cent.

These statistics, though they indicate a relatively low percentage of "cures," appear quite favorable when viewed in the light of the poor clinical material from which they were obtained, and the fact that they were operated upon by 34 different surgeons.

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NIPPLE DISCHARGE

A CLINICOPATHOLOGIC STUDY

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THIS report is based upon a study of 67 patients, who had a discharge from the nipple. All types of nipple discharge were included because our experience demonstrated the danger of focusing attention on bloody discharge only. The cases were found by reviewing records of all breast cases seen in the Tumor Clinics of the Massachusetts General Hospital and the Boston Dispensary. From May, 1925, to January, 1939, 69 cases, or 7.6 per cent of 898 patients seen in the Massachusetts General Hospital Tumor Clinic, had nipple discharge. From January, 1932, to December, 1938, 19 cases, or 12.4 per cent of 153 patients at the Boston Dispensary Tumor Clinic, had nipple discharge. Thus, 8.3 per cent of 1,051 patients coming to the two clinics had nipple discharge. Excluded from this series are patients with discharge from inverted nipples, and patients with Paget's disease in whom a discharge came from an ulcerated nipple. In only 67 cases of a total of 88 were the records and clinical data adequate to warrant their inclusion in this report.

In 52 instances, operation had been performed. Slides were reviewed in all but five of these cases. In 15 cases, either no surgery had been advised, or the proffered surgery had been refused, but all these patients were under observation for a period sufficient to justify inclusion. In several patients a positive diagnosis of carcinoma of the breast was established by the clinical course which subsequently progressed to a fatal termination. The composition of a series of patients with nipple discharge, who come to a Tumor Clinic, is not altogether representative, because a number of patients and doctors find their own solution to the problem, unless the discharge is bloody or a tumor is also present.

Discharge from the nipple may be discussed under three headings: (1) Frequency. (2) Type of discharge. (3) Etiology of discharge.

Frequency.—Some type of discharge from the nipple occurs in about 8 per cent of all mammary lesions. A sanguineous discharge occurred in 6 per cent of 5,118 patients coming to the Johns Hopkins Hospital because of a breast complaint.[30] Deaver and McFarland[21] stated that 3 to 5 per cent of breast cancers are accompanied by a discharge. Geschickter[29] reported a bloody nipple discharge in 96 of 204 cases (47 per cent) of duct papilloma. In a series of chronic mastitis cases, MacCarthy and Mensing[61] found that 6.6 per cent of 406 patients manifested a discharge from the nipple.

Type of Discharge.—Certain generalizations are valid. A sanguineous dis-

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charge should arouse more concern than a nonsanguineous one. When a duct papilloma is responsible, discharge is often serosanguineous. A dark, bloody discharge is commonly caused by a duct carcinoma. However, too much emphasis must not be placed on such correlation. It is particularly important to appreciate that the presence of a carcinoma cannot be excluded because the discharge is free of blood. Two forms of breast discharge have diagnostic significance: (1) A grumous, greenish yellow discharge is almost always due to stasis in dilated ducts. (2) A continuous, milky discharge, often bilateral, is galactorrhea. The incidence of various types of discharge in this study is shown in Table I.

TABLE I

INCIDENCE OF TYPES OF DISCHARGE

Bloody (including serosanguineous)	36 (54%)
Serous	16 (22%)
Milky	5 (7%)
Watery	2 (3%)
Miscellaneous	8 (13%)

Etiology of Discharge.—The experience of a number of investigators has shown that the three most common causes of discharge from the breast are duct papilloma, carcinoma, and chronic cystic mastitis, in that order of frequency. If bloody discharge only is studied, slightly more than one-half of the cases are due to a benign lesion. The incidence of chronic mastitis, as the cause of a bloody discharge, ranges from 7 per cent (Adair) to 15 per cent (Geschickter). Since this report deals with all types of discharge, it is not surprising to find that chronic mastitis was the etiologic factor in 27 per cent of our cases.

Other conditions may be enumerated. Nonspecific infections of dilated ducts are often accompanied by nipple discharge. Clinical evidence suggests an endocrine factor in some cases, although Taylor[80] was unable to confirm this by laboratory studies on a large group of women. Rare causes are trauma, sarcoma, fibro-adenoma, luetic and tuberculous mastitis. Table II shows the causes of discharge in our 67 patients, eight of whom had bilateral discharge.

TABLE II

CAUSES OF NIPPLE DISCHARGE IN 67 PATIENTS

Carcinoma (excluding Paget's disease)	22 (33%)
Paget's disease	2 (3%)
Chronic cystic mastitis	18 (27%)
Duct papilloma	7 (10.5%)
Hormonal dysfunction	7 (10.5%)
Inflammatory cysts	3 (4%)
Fibrous mastitis	2 (3%)
Miscellaneous	6 (9%)
Total	67

In 15 patients not operated upon, only a clinical diagnosis was available. However, in any similar group, there will be a number of patients in whom no indication for surgery is apparent, yet reasonably accurate diagnoses may be made. This source of error was minimized by the exclusion from this report of 24 patients whose records were inadequate.

Pathology.—About 75 per cent of the cases of nipple discharge are due to three lesions: (1) Carcinoma; (2) papilloma; and (3) the proliferative phase of cystic disease of the breast (Schimmelbusch's disease or adenosis). The carcinomata associated with nipple discharge are often the more localized, slowly growing papillary or comedo types. The majority of papillary carcinomata are thought to represent a late development in preëxisting benign papillomata. Geschickter noted that about one-third of the comedo carcinomata in his series (106 cases) occurred "in breasts which were the seat of adenosis." It is our opinion that this phase of cystic disease of the breast is a precancerous lesion, as is the duct papilloma, but to a lesser degree.

A fairly well standardized attitude prevails toward abnormal discharge from other body orifices, particularly a bloody discharge. No such agreement exists with regard to nipple discharge, bloody or otherwise. It is the purpose of this communication to stress the importance of nipple discharge as a sign which should make the observer search for an actual carcinoma or a precancerous lesion in the affected breast. In many cases, neither will be found, but only by such search is the patient's welfare adequately safeguarded.

Duct papilloma is widely acknowledged to have a potentiality for carcinomatous degeneration. Controversy centers upon chronic cystic mastitis and especially the actively proliferating lesions characterized by epithelial overgrowth in dilated ducts and small cysts (Schimmelbusch's disease, adenosis of Lewis and Geschickter,[56] cystipherous desquamative epithelial hyperplasia of Cheatle and Cutler)[14] (Fig. 1). In the literature, there is scant attention given to this lesion as a cause of discharge from the nipple. Auchincloss[3] stated that unexplained nipple discharge occurs most often from breasts containing cysts with epithelial proliferation. He added that this is the group of benign breast lesions most commonly associated with cancer. Geschickter reported that 47 of 211 benign cases of bloody nipple discharge were due to this lesion. Robles and Banno[73] declared that it was the most frequent type of benign lesion associated with bleeding from the nipple.

The consensus of present opinion holds that cystic disease, in general, is not a precancerous state. However, there is accumulating an increasing volume of evidence to suggest that cystic disease with epithelial hyperplasia is precancerous, although the supervention of malignancy may occur less frequently than is the case with the papilloma. In Warren's[84] recent study in which he concludes that chronic cystic mastitis predisposes to the development of breast cancer, he stresses the importance of this epithelial hyperplasia. Such cases comprise about 14 per cent of all cases of cystic disease of the breast, according to Lewis and Geschickter,[58] and 9 to 12 per cent of them show nipple bleeding.

In our series, 13 women were proven, histologically, to have chronic cystic mastitis. Ten of the specimens were associated with epithelial hyperplasia. Four of our patients were over 55 years of age. The slides from these four cases were shown to four Boston pathologists, all of whom regarded the lesion as precancerous. Moreover, histologic study of the 22 breast cancers with

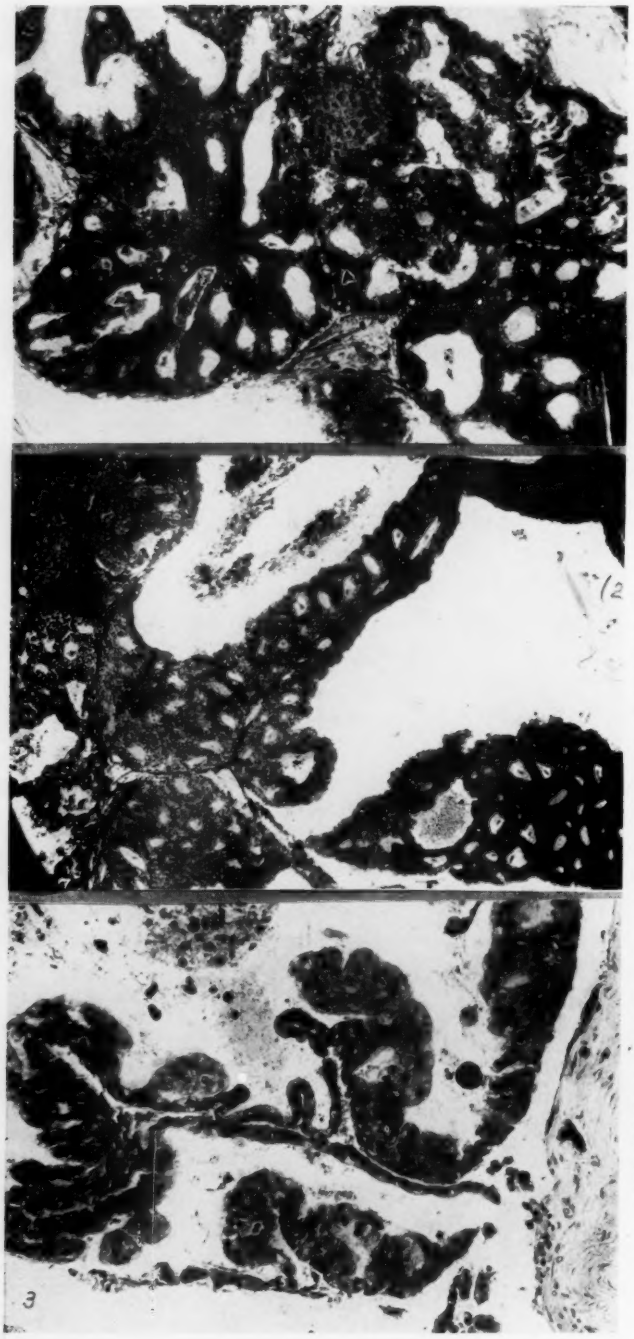

FIG. 1.—Case G. T. (M.G.H. East Surgical, No. 332503): Section shows the proliferative phase of chronic cystic mastitis (Schimmelbusch's disease or adenosis). This breast contained many small cysts. Note the benign papillary hyperplasia. The patient was 55 years of age. Pathologists to four large Boston hospitals were unanimous in regarding this lesion as precancerous. (X180)

FIG. 2.—Case M. M. (B. D., No. 228908): Section showing dilated ducts lined by hyperplastic epithelium. This is Schimmelbusch's disease. In the same area of the breast, there was also a metastasizing adenocarcinoma, which could not be felt prior to operation. (X180)

FIG. 3.—Case B. E. (B. D., No. 346749): This patient was 65 years old. This section was diagnosed as chronic cystic mastitis with marked intraductal epithelial hyperplasia. In the opinion of Dr. Shields Warren, pathologist, this lesion was definitely precancerous. A simple mastectomy was performed. (X240)

nipple discharge revealed that in six cases there was a marked degree of similar epithelial hyperplasia within the ducts, located in the same sector of the breast, in which the invasive, neoplastic epithelium had been found. In two of the six, the diagnosis of comedo carcinoma was warranted. In two other cases, the pathologist had already commented upon the presence of the Schimmelbusch type of proliferating epithelium seen in the same slide in which the carcinoma was present. Cheatle[14] argues that this more than occasional coexistence of Schimmelbusch's disease and carcinoma is not mere coincidence. Warren's careful appraisal of their relationship led him to believe that the former condition predisposed to the latter. Geschickter,[29] who has been a strong advocate of the benignancy of chronic cystic mastitis, recently acknowledged that about one-third of the comedo carcinomata in his series occurred in breasts which were the seat of adenosis. The study of our clinical and histologic material has aroused the conviction that this epithelial overgrowth has a potentiality for malignant degeneration.

In an analysis of the 67 patients considered in the present study they were divided into eight groups according to etiology. These groups will be discussed in order of their frequency.

Carcinoma.—Twenty-four of 742 cancers of the breast (3.2 per cent) were accompanied by some form of discharge from the nipple. Two of these were Paget's disease. The average age was 50 years. Ten of the remaining 22 women had a bloody discharge, while 12 had a nonsanguineous discharge. In five cases the discharge was regarded as incidental, usually because it was very slight in amount and appeared long after the obvious tumor. In 17 cases the discharge was significant. A study of these 17 women is profitable. In a number of instances, the correct diagnosis was not established until long after the onset of the discharge. Four common sources of diagnostic error were apparent: (1) The youth of the patient; (2) the fact that the discharge was not bloody; (3) the discharge was the first symptom; and (4) the absence of a palpable mass in the breast.

(1) Two young women, 32 and 26 years of age, had bloody nipple discharge, painful breasts, but no mass when first seen. In both, the affected breast was described as "shotty," and in one patient this nodularity was localized in the upper, outer quadrant. Such localized nodularity Cutler[17] proclaims as "a sign of great gravity," signifying the Schimmelbusch stage of chronic cystic mastitis. In one case three years elapsed before the discovery of an axillary metastasis brought about radical mastectomy, and the disclosure of an impalpable carcinoma (Fig. 2). This tumor was situated in an area of marked intraductal epithelial proliferation. In the second case, mastectomy performed one year later because of increasing nodularity demonstrated a comedo carcinoma with early invasion.

(2) There appears to have been undue emphasis on the bloody nature of nipple discharge. It is noteworthy that more than one-half the patients with cancer, in this study, had a discharge which was at no time bloody. Four women had a serious discharge. In three of them, a clinical diagnosis of

chronic cystic mastitis had been made despite the presence of a mass in the breast. This suggests that the absence of blood in the discharge persuaded observers that the lesion was benign.

Case Report.—M. G. H., East Surgical, No. 291743: G. L., female, age 25, who had been under treatment for pelvic inflammation, was found to have a discharge of thick serum coming from her right breast in which four separate nodular areas were present. A diagnosis of chronic cystic mastitis was made. Four months later she was first examined in the Tumor Clinic. Operation disclosed a rapidly growing cancer from which the patient died in two years.

(3) In 11 women, a discharge from the nipple had been the first indication of pathology in the breast. At their first Tumor Clinic visit seven of them also had a mass. The discharge preceded detection of a breast mass in these seven cases by an average of 12 months. Early cancer of the breast is more commonly associated with a discharge from the nipple than with any other sign except the presence of a lump. It is the first sign in about 1 per cent of all breast cancers.

(4) Four women had no palpable tumor in the breast when first examined. Three of them had a bloody discharge. All four breasts were abnormal, two showing localized nodularity in the upper outer quadrant, the other two presenting diffuse lumpiness. The four women had been observed for periods ranging from eight months to four years, before the diagnosis of cancer was established. Two young women received a small amount of roentgenotherapy to the breast, as suggested by Adair[1] in 1931. Discharge lessened but did not cease. In three of these four patients, the periodic clinic notes detail a steadily progressing process in the upper outer quadrant, with increasing confluence of nodularity, culminating in a demarcated area of induration which compelled biopsy. In the fourth case, no breast tumor was detected but an axillary metastasis required surgical intervention.

We concur with Wainwright's[83] dictum that the entire breast should be removed in those cases of nipple bleeding wherein no localized focus is clinically demonstrable. The bleeding breast with no tumor must be suspected of harboring not only a papilloma or precancerous epithelial hyperplasia, but even an actual, impalpable carcinoma.

Chronic Cystic Mastitis.—There were 18 cases of chronic cystic mastitis. In five patients, the diagnosis was based upon clinical evidence only. The discharge was bloody in seven women, serosanguineous in four, serous in four, and three women had a milky, a greenish, and a brownish discharge, respectively. The average age was 44. The physical findings were variable. Only three cases conformed to the clinical picture of Schimmelbusch's disease (*i.e.*, localized nodularity). However, clinical detection of this menacing phase of cystic disease is unreliable. Ten women had intraductal papillary epithelial hyperplasia. The nipple discharge contained blood in nine of these ten.

Case Report.—B. D., Tumor Clinic, No. 2449: M. A., female, age 42, had had simple mastectomies at a three-year interval, because of bloody nipple discharge. Neither breast was abnormal to palpation. However, in one breast there was marked papillary

proliferation, whereas its mate contained only a few small, blue-domed cysts and increased connective tissue.

Whatever concessions one may make to the general proposition that cystic disease is not precancerous, marked epithelial growth in the breasts of elderly women must occasion alarm. Two women, 68 years of age, are illustrative.

Case 1.—B. D., No. 329407: E. C. had manifested nipple bleeding for six months. No tumor was palpable. A radical mastectomy was performed because of the pathologic report—intracanalicular papillary adenocarcinoma. However, a review of the slides shows a benign lesion consisting of papillomatous infoldings of hyperplastic epithelium, with normal cell detail, and no invasion.

Case 2.—B. D., No. 346749: B. E. had had a lump in the breast for five years, intermittent, yellowish discharge. There was a diffuse, indurated area lateral to the nipple. A clinical diagnosis of Schimmelbusch's disease was confirmed microscopically. It was the opinion of Dr. Shields Warren,[84] who has recently published a study of this problem, that the lesion was to be regarded as precancerous, not only with respect to comedo carcinoma, but also to ordinary infiltrating carcinoma (Fig. 3).

The conclusion seems warranted that in cases of nipple discharge associated with a nodular breast, particularly if the discharge contains blood, the majority of such breasts will show epithelial hyperplasia. The disposition of this group will depend upon the surgeon's attitude toward the life history of such epithelial activity.

Duct Papilloma.—Seven duct papillomata were found. In the literature, papilloma and carcinoma have an equal rôle in accounting for about 90 per cent of the cases of bloody nipple discharge. The papillomata are located in the larger ducts, often under the areola. They are often bilateral and are multiple in the same breast in about 30 per cent of the cases. A nipple discharge, usually serosanguineous, occurs in 50 per cent. The lesion is frequently impalpable but may be detected by transillumination, if bleeding has occurred, as the blood delineates the papilloma. Sometimes the diagnosis can be made by detecting a small area of thickening under the areola, pressure on which evokes the nipple discharge.

Adair has estimated that the supervention of carcinoma requires 10 to 12 years. By that time a palpable mass is almost always present. However, there have been a number of cases in which the malignant transformation had occurred, yet the only evidence of its presence was the discharge from the nipple. Bloodgood, who has said that a woman with nipple discharge and no tumor runs no more risk of cancer than a woman who has neither, nevertheless sought for and removed papillomata even although impalpable.

Two of our seven patients had a nonsanguineous discharge. Six simple mastectomies were performed, but frequently the lesion can be removed by local excision. In a seventh patient, the diagnosis was made by transillumination. On microscopic study, the diagnosis of a benign lesion is occasionally difficult.

Case Report.—M. G. H., East Surgical, No. 298127: M. A., female, age 32, had had occasional slight bleeding from left nipple for 12 years. Examination showed a small,

hard mass underneath and adherent to the areola. The original pathologic diagnosis was papillary adenocarcinoma of low malignancy. However, current review of the sections demonstrates that the lesion is benign (Fig. 4).

In the 22 breast carcinomata in this study, there were three in which the clinical evidence and pathologic appearance suggest their origin in a pre-existing benign papilloma (Fig. 5).

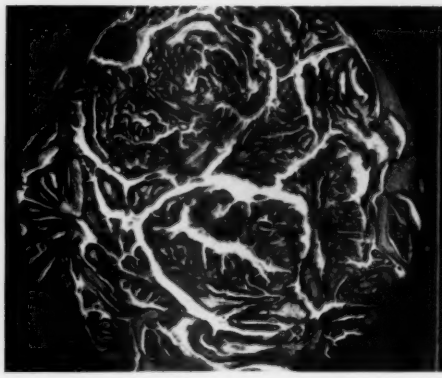

FIG. 4.—Case M. A. (M. G. H., East Surgical, No. 298127): Section shows a benign papilloma. There is no invasion, despite a 12-year history of nipple bleeding. (X120)

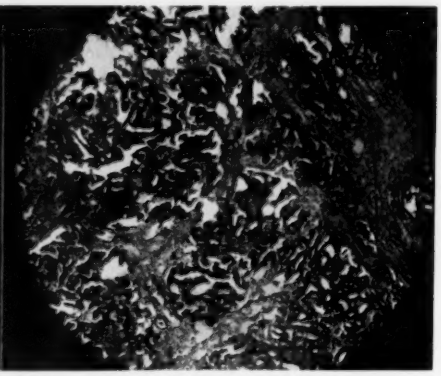

FIG. 5.—Case L. M. (M. G. H., West Surgical, No. 281571): A papillary adenocarcinoma with nipple discharge and a mass underlying the nipple. (X120)

Discharge from Hormonal Dysfunction.—The indications for inclusion of cases under this heading are not altogether satisfactory, since they rest on clinical grounds only. None of these seven patients was operated upon. There were no masses, cysts, nor areas of nodularity in any of these breasts. Three women had a milky discharge; three had a brownish or serosanguineous discharge; and one woman had a mucous discharge which ceased after the administration of ovarian extract. Mazer[63] and Lewis and Geschickter[56] have reported good results after estrogen therapy in a small group of women in whom breast bleeding occurred at the time of menopause. They postulate a lobular proliferation of epithelium (*i.e.*, adenosis) due to deranged hormonal physiology, and have clinical and experimental evidence in support. However, their therapy rests upon the clinical diagnosis of the morbid state in the mammary gland. In our experience, the clinical diagnosis in this age-group is not to be relied upon to this extent.

Nathanson[68] has demonstrated a definite relationship between galactorrhea and deficiency of the estrogenic hormone. The proliferative action of estrin on the epithelium of the cervix is well known. Our cases of galactorrhea warrant mention in this connection. The three women were multiparae, with badly lacerated, infected cervices. Two of them were given large amounts of estrin over a period of months, during which time the galactorrhea ceased. In one woman, a small, infiltrating carcinoma of the cervix was discovered one year after treatment was started. In the second patient, a biopsy of the cervix, ten weeks after treatment, showed "some growth of epithelial cells

between the columnar epithelium, and the basement membrane" which was regarded as a possible precancerous focus. It is suggested that a conservative attitude toward the administration of large amounts of estrin for the correction of this breast discharge is perhaps wise, particularly if there is other pathology in the breast or cervix.

Paget's Disease of the Nipple.—It is of course recognized that Paget's disease will often be attended by a discharge from the surface of the ulcerated nipple. However, a number of investigators, including Jacobeus,[44] Dunn,[24] and Muir,[67] have advanced the proposition that a carcinoma of the large ducts precedes and eventually causes the characteristic nipple changes. In such an event, it is logical that the intraductal growth might manifest its presence by nipple discharge, prior to the appearance of the "pagetoid" changes in the nipple.

From a number of instances of Paget's disease, two cases were found in which a nipple discharge antedated any observed alteration in the nipple. The discharge was bloody in one case, and "watery-yellow" in the second. Lepper and Baker[59] reported a bloody discharge in 7 of 11 intraductal carcinomata. Geschickter describes 25 cases of duct cancer composed of large "pagetoid" cells, seven of which manifested nipple discharge in the absence of nipple ulceration.

Inflammatory Cysts.—A diagnosis of inflammatory cyst had been made on three specimens. The patients were 31, 40, and 48 years old, respectively. All three presented a circumscribed mass in the central portion of the breast for which they had been referred to the Tumor Clinic. In addition some type of nipple discharge, varying from bloody to milky, was also present. On pathologic examination, isolated chronic cysts with smooth lining were found. The cyst walls showed pronounced inflammatory changes.

Fibrous Mastitis.—Two breasts in this series, which were removed because of bloody discharge, showed histologically a pronounced increase in breast stroma accompanied by apparent atrophy of the epithelial elements. A female, age 33, gave a history of breast pain for one year, and bloody nipple discharge for four months. Clinically, her breast was unremarkable. On section, it was dense, leathery, and firm. There were no cysts. Microscopically, a profound fibrous mastitis, with atrophy of epithelial structures, was seen.

A female, age 71, had had a milky nipple discharge, followed by a reddish-brown discharge for eight months. Her breast was small, firm, and the nipple was hard and inverted. Sections, studied microscopically, were comparable to the above case.

The elderly patient should probably be classified as an example of senile involution. A precocious involution may also be responsible for the changes in the breast of the younger woman. Chronic interstitial mastitis, which Ewing[26] describes as a variant of chronic mastitis, is not usually marked by this degree of epithelial atrophy.

It is of interest to note that the sign of nipple bleeding, so commonly asso-

ciated with hyperplastic epithelium, can also occur in a breast in which there is minimal epithelial activity.

Miscellaneous.—Under this heading are included six cases which have been under recent observation and in which the diagnosis has not been clearly established. With one exception, all of these patients are from 35 to 40 years of age. Three of them have had serosanguineous discharge, and three have had only a serous discharge. Two women in this group illustrate certain features of special interest:

Case 1.—B. D., No. 316809: H. M., female, age 36, had had a bloody discharge for three weeks. A minute mass could be felt just superior to the areolar margin. This mass had also been felt in another Tumor Clinic. Survey was urged but refused. Three months later the tumor was no longer present and no discharge had occurred.

It is probable that a bleeding duct papilloma was responsible. The tumor resulted from an accumulation of blood in a cystic dilatation of a duct. With cessation of bleeding, the small cysts collapsed. Fischer,[27] in 1931, cited an instance of a "phantom tumor of the breast" produced in this manner.

Case 2.—M. G. H., Unit No. 33065: M. S., female, age 17, had had bloody nipple discharge intermittently for one year, following trauma to the breast. On examination, the breast felt normal, and no discharge could be expressed. Transillumination was not carried out.

While trauma is a well-recognized cause of bloody nipple discharge the relationship is usually obvious—a hematoma is present, and bleeding ceases within two weeks after the trauma. Therefore, a number of authors lay stress upon repeated or continuous bleeding as opposed to a single, brief episode. Thus, it is improbable that trauma played a principal rôle in the last case (Case 2).

Diagnosis.—(A) Nature of the Discharge: A thick, inspissated discharge may come from inverted nipples. Microscopic examination is often necessary, in order to demonstrate the presence of blood, as Adair has emphasized, but is of no help in revealing the presence of malignant cells, according to Greenough.[34] The presence of blood is significant, but its absence cannot rule out a lesion dangerous to the patient. Diagnosis is practically established by the finding of a continuous milky, or a greenish yellow discharge, indicating respectively, galactorrhea or duct stasis.

(B) Source of Discharge: Three special diagnostic aids are employed for the detection of lesions associated with nipple discharge. The presence of a small lesion, such as a papilloma, is occasionally demonstrated by the positive pressure test, whereby pressure over a segment of the areola expresses the discharge from the nipple. Transillumination will distinguish between a solid tumor and a cyst containing clear fluid, and will often reveal impalpable papillomata which may be multiple. However, if the papilloma has not bled, it may escape detection, as the opacity seen on transillumination is usually due to the collection of blood around it. Recently, the value of contrast mammography has been acclaimed, especially by Hicken and his co-workers.[42] Our experience with the method has been limited to a few cases. The serious

tissue reactions which several groups of investigators have reported following the use of thorotrast for mammography, plus the possibilities of diagnostic error, tend to minimize its value.

Treatment.—The group of patients in whom both tumor and discharge are present arouse no controversy. The presence of the mass is an indication for surgery, independent of discharge. However, a bloody discharge should not stampede the surgeon into performing a radical mastectomy. In Hart's[40] series of 104 benign, intracystic papillomata, a radical mastectomy had been performed in 38 per cent. On the other hand, Miller and Lewis[65] found 27 malignant lesions in 40 breast tumors associated with nipple bleeding. Frozen section diagnosis of lesions associated with nipple discharge is sometimes difficult, because early or uncommon types of cancer may be encountered for the diagnosis of which permanent sections may be necessary.

The troublesome and dangerous problem is the discharging breast which, on examination, contains no mass. DaCosta[19] has said, "It is better that a woman lose her breast needlessly, than her life." One need offer no apology for performing many biopsies or even simple mastectomies in border-line cases wherein the clinical picture suggests the possibility of carcinoma, even though many such operations demonstrate a benign lesion. However, the psychic and cosmetic arguments against mastectomy are prominent in the minds of patients, and demand consideration. Three general alternatives present themselves.

(I) *Mastectomy.*—Cheatle[12] is a strong advocate of mastectomy when the discharge is bloody. Supporters of this policy argue that the undiscovered source of the discharge is probably a papilloma or Schimmelbusch's disease, both of which they regard as precancerous. Moreover, the first sign of an actual cancer may be nipple discharge.

(II) *Observation.*—Bloodgood[5] has stated that bleeding *per se* never justifies complete removal of the breast. Adair's recommendations are conservative. He has given up irradiation for this group of cases and awaits the appearance of a tumor unless transillumination reveals a papilloma. Geschickter, and others treat adenosis with large doses of estrin. Nodularity and bleeding often disappear. In favor of a waiting policy are the facts that impalpable cancer is rare, and discharge, even though bloody, not infrequently ceases spontaneously. Moreover, many surgeons do not regard this proliferative phase of cystic disease as precancerous.

(III) *Local Excision or Mastectomy.*—To many women, the idea of a mastectomy is intolerable, and in many cases of nipple discharge it is a radical procedure. Local surgery may often supplant the less desirable alternatives of observation or mastectomy. There are five groups of patients with nipple discharge and no tumor, in which the indications for surgery are definite, in our opinion:

(1) Nipple discharge with positive transillumination.
(2) Nipple discharge with positive pressure test.
(3) Nipple discharge with localized nodularity in the breast.
(4) Nipple bleeding after the menopause.
(5) Continued nipple bleeding of undetermined origin.

(1) *Nipple Discharge with Positive Transillumination.*—When transillumination demonstrates an area of opacity in one of the large ducts near the nipple, the probable diagnosis of papilloma may be made. Local excision of the offending duct is indicated. The ingenious suggestion of Babcock[4] appears to be the most satisfactory procedure for identifying the diseased duct in the operative field. Noting the duct orifice in the nipple whence the discharge comes, he threads the duct over the blunt end of a fine needle. An incision is made at the areola margin and the duct is distinguished by tilting the inserted needle. Multiple opacities may be visualized. Block excision of a breast segment or mastectomy may be required, depending on the extent and distribution of the papillomatous lesions.

(2) *Nipple Discharge with Positive Pressure Test.*—Occasionally, palpation and transillumination are negative, but pressure over a constant area within or near the areolar zone produces the discharge. A recent clinic patient had had amber-colored nipple discharge for one year, bloody on one occasion. She was able to cause the discharge by drawing a finger tip across the areola toward the nipple, along a constant axis. The discharge came from only one duct orifice. Palpation and transillumination were negative. In our opinion, excision of this duct should be undertaken.

(3) *Nipple Bleeding with Localized Nodularity in the Breast.*—Not infrequently, bloody nipple discharge occurs in a woman about 40 years of age, whose breast, on palpation, manifests a localized area of nodularity commonly felt in the upper outer quadrant. The remainder of the breast may be normal, or there may be diffuse "shottiness" in which one area stands out more prominently than the rest. Histologically, such an area is apt to present the picture of epithelial overgrowth. Twice in our experience, this clinical appearance of a benign lesion has masked the presence of an actual carcinoma in this site. It is our conviction that a biopsy should be obtained in all such cases. If hyperplastic epithelium is found, either a quadrant excision or mastectomy is proper.

(4) *Nipple Bleeding after the Menopause.*—In this situation, the psychic and cosmetic arguments against mastectomy are so attenuated, and the threat of cancer so real, that it is safer to adopt an arbitrary policy and advise simple mastectomy, unless it is possible that some definite local lesion can be identified.

(5) *Continued Nipple Bleeding of Undetermined Origin.*—The entire breast should be removed in those cases of continued nipple bleeding (*i.e.*, one month or more) in which no localized source of the bleeding is apparent.

Further aid in individualizing patients with a breast discharge as to surgery versus observation may be secured by a consideration of the following factors: (1) The type of discharge; (2) the duration of the discharge; (3) the age of the patient; (4) a family history of cancer; (5) the size of the breast; (6) the psychology of the patient; and (7) the question of adequate follow-up, essential to a program of observation.

SUMMARY AND CONCLUSION

(1) Sixty-seven cases of nipple discharge are reported. The discharge contained blood in 35 instances.

(2) Three lesions were responsible for about three-quarters of the cases—carcinoma, chronic cystic mastitis, and papilloma. The papilloma is a precancerous condition. Chronic cystic mastitis, with epithelial hyperplasia, is also to be regarded as precancerous.

(3) Twenty-four women had cancer. Twelve of them had a nonsanguineous discharge. In 11 women, discharge was the first warning of any disease in the breast. Four women had no mass in the breast at the time of their first examination.

(4) Contrary to common experience, chronic cystic mastitis was encountered more than twice as often as papilloma.

(5) The chief problem in this study is the discharging breast in which no mass is palpable. Such a breast must be suspected of harboring not only the precancerous conditions of a papilloma or chronic cystic mastitis with epithelial hyperplasia, but even an actual cancer.

(6) Treatment consists of local surgery or mastectomy. Radiation therapy has not proven to be of value. A definite number of cases require not operation, but observation; the surgeon, however, should try to make this latter group as small as possible, by consideration of all possible surgical indications. In this manner, important cancer-preventive surgery can be performed and the surgeon will occasionally be rewarded by the discovery of an early, impalpable cancer.

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SURGICAL TREATMENT OF TUMORS OF THE MEDIASTINUM*

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THE MEDIASTINUM harbors an extraordinary variety of tumors and tumor-like lesions. These include the dermoid cysts and teratomata, the cysts of endodermal and mesodermal origin, the cystic lymphangiomata, and the echinococcus cysts; the connective tissue tumors including the fibromata, lipomata, leiomyomata, xanthomata, chondromata, chondromyxomata and chondromyxosarcomata; the neurogenic tumors including the neurofibromata, ganglioneuromata, neuroblastomata and neuro-epitheliomata; the primary tumors of the thymus including the benign and malignant thymomata; the primary tumors of the mediastinal lymph nodes including lymphosarcomata, Hodgkin's disease and endotheliomata; the primary and secondary sarcomata of the mediastinum; the rather heterogenous group of primary and metastatic carcinomata of the mediastinum; and, lastly, the intrathoracic goiters. These form unusually interesting groups of pathologic lesions, to each of which much more time could profitably be devoted. Their surgical treatment is a large subject which cannot properly be discussed briefly; and in a short résumé of the surgical procedures employed one can only make some broad and general statements, to which, no doubt, many may find exceptions from their own experience.

Except to name the varied tumors of the mediastinum as above mentioned, their pathology will not be further considered. Symptomatically, all tumors of the mediastinum give rise to somewhat similar clinical manifestations. These may be grouped as general symptoms because they are common to all tumors and include pain in the chest, cough, dyspnea and cyanosis; and local symptoms caused by pressure upon or involvement of structures in the immediate neighborhood of the lesion. These latter give some indication of the location of the lesion within the mediastinum; and since certain tumors have a predilection for certain locations, give us also some indication of the nature of the lesion. The occurrence of Horner's syndrome, for example, suggests not only a lesion of the posterior mediastinum, but one arising from the paravertebral sympathetic chain. It is to be noted, however, that mediastinal tumors may fail to give rise to noteworthy symptoms. With the more frequent use of routine roentgenologic examinations of the chest, an increasing number of individuals are coming under observation who have mediastinal tumors but who fail to have symptoms referable to them.

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In the diagnosis and differential diagnosis of mediastinal tumors all the available resources of the internist, roentgenologist, bronchoscopist and surgeon often are necessary. Often physical, roentgenologic, bronchoscopic, sputum and other examinations will serve, in some cases, not only to establish the presence and location of a lesion but also its pathologic nature. In other cases, the application of these diagnostic measures succeeds in establishing the presence of a lesion, but fails to indicate its nature. In some of these, and especially those near the thoracic wall, an aspiration biopsy may serve to establish the pathologic diagnosis; in others, the removal of an accessible involved lymph node; in still others the response of a lesion to a controlled dose of roentgenotherapy. But there will remain, in any series, a number of cases in which all diagnostic measures now available to us fail to establish the pathologic nature of the tumor. In these, nothing short of an exploratory thoracotomy will establish it. Certainly, one of the handicaps to more intelligent treatment of mediastinal tumors lies in our diagnostic limitations.

Surgical Indications.—It has been our experience that the dermoid cysts and nonmalignant teratomata, the various other mediastinal cysts, the intrathoracic goiters, the benign connective tissue tumors, including those derived from cartilage, the benign tumors of neurogenic origin, the benign tumors of the thymus and some of the sarcomata lend themselves to surgical removal; while, thus far in our experience, the primary malignant tumors of the mediastinal lymph nodes (lymphosarcoma, Hodgkin's disease, *etc.*), the malignant teratomata, the malignant thymomata and the various other mediastinal carcinomata have proven unsatisfactory from the viewpoint of surgery. While a number of such cases have been subjected to surgery, exploration has always shown an extent of the disease beyond the possibilities of surgical eradication. Roentgenotherapy in these has served to relieve the symptoms and prolong life, particularly in patients with Hodgkin's disease and lymphosarcoma, but in our hands has not proven very helpful in other lesions within the mediastinum.

If, then, a positive diagnosis can be made of the various benign tumors and cysts which I have enumerated, surgical removal is believed to be the treatment of choice. If, on the other hand, a positive diagnosis can be made of the malignant lesions I have just mentioned, surgery has not, as a rule, been attempted. In cases in which the diagnosis cannot be established and which may be benign or malignant, certain criteria have been used in deciding for or against operation. Most important, in our hands, in deciding for operation is the character of the shadow seen in the roentgenogram. A clearly defined, circumscribed shadow is most often associated with a benign lesion although it does not rule out a ganglioneuroma or teratoma which has undergone malignant change, nor certain sarcomata, nor lesions other than tumor, as mediastinal abscess, nonpulsating aneurysms, *etc.*

In reviewing our experience, I find that there is a great difference of opinion with respect to the treatment of tumors without, or with insignificant, symptoms with respect to the roentgenotherapy of mediastinal tumors, and

with respect to the size of tumors which may be attacked surgically. These aspects of surgical indications deserve, perhaps, a brief discussion.

There seems little doubt that various benign mediastinal tumors may fail to provoke pronounced symptoms over long periods of time. The occasional finding, in an elderly individual, of a tumor which, because of its nature, must have originated early in life, even suggests that a person may carry a tumor throughout life without serious impairment of health. But our experience and that of others, as reported in the literature, is that this is exceptional rather than common. The early or late appearance of symptoms in any given case is dependent upon the relation of the tumor to important mediastinal structures. The general symptoms of pain, cough, dyspnea and cyanosis and the local pressure symptoms manifested, for example, by Horner's syndrome, are the results of compression or involvement of important blood vessels, nerves, trachea, bronchi or esophagus within the mediastinum. A tumor may be so placed with respect to these structures as not to involve them; and symptoms may be inconspicuous or absent. Again, a small tumor, placed so as to compress a major bronchus, may cause the most intense symptoms, while another tumor of unbelievable size may cause only moderate symptoms. There is some evidence to show that some benign tumors undergo a slow and continuous growth, as might be expected; while others, having reached a certain size, become, for a considerable time, quiescent, or grow so slowly that their growth cannot be demonstrated roentgenographically over several years. These presumably quiescent tumors may at any time again begin to grow and this secondary activity may, and not uncommonly does, indicate a malignant change in a previously benign tumor. In general, I think it may be said that the tumors without symptoms, or with insignificant symptoms, sooner or later provoke symptoms because of simple enlargement or malignant degeneration. A study of our cases, and a review of the literature, show the danger to the individual who harbors a benign tumor. In a review of more than 150 dermoid cysts I find that 46 remained untreated; all died of the disease; among 13 cases of dermoid cyst and teratoma in our own series, five had undergone malignant change at the time they came under our observation. Of 28 cases of lipoma of the mediastinum, 13 were not treated and all died; and in seven death was directly due to the lesion. In 18 cases of fibroma of the mediastinum, 13 were not treated and all died; in five, the tumor was removed and all recovered. I could enlarge upon data such as these. The point I wish to make is that the lack of prominent symptoms in a patient with a mediastinal tumor is, to the individual, a fortunate circumstance, but does not necessarily imply that the lesion is quiescent, or that it may not undergo malignant degeneration, or that it may not eventually cause death if not removed. It would seem wise, at least, to seriously consider surgery in this group of cases.

With respect to the roentgenotherapy of tumors of the mediastinum, it has been our experience that a majority of patients referred to us have already had deep roentgenotherapy for their lesions. The opinion seems

to be prevalent that roentgenotherapy may achieve satisfactory results in mediastinal tumors; and if it fails to do so, surgery may then be considered. I would suggest that this attitude be reversed; that upon the discovery of a mediastinal tumor, the surgeon, experienced in this field, should first be consulted; and not until he has concluded that surgery is inadvisable should roentgenotherapy be undertaken. It has been found, as I have indicated, that certain benign tumors and a few of the malignant tumors of the mediastinum are amenable to surgical removal. These, in general, fail to respond to roentgenotherapy. Not only does roentgenotherapy fail to reduce their size but it may also fail to prevent their malignant degeneration. It may and does provoke massive adhesions in the mediastinum which make later surgical removal more difficult and dangerous. In these cases roentgenotherapy is not only a wasted effort but one which may actually do harm.

The mere size of intrathoracic tumors has, on occasion, deterred the physician from contemplating the possibility of surgery. Reading the reports in the literature, one comes across cases of large tumors which are frequently mediastinal in origin. They have died from mediastinal compression, and the autopsy records the presence of a large mass unattached to any vital structure and easily removable. Some authors, in their comments upon such cases, have expressed regret that they had not considered the possibility of surgery. Our small experience with large tumors indicates that they may be removed. The duration of symptoms, the finding of a circumscribed shadow, and the fact that the patient has not long since succumbed to the condition, implies that the lesion is benign and has not involved vital structures within the mediastinum. Their removal is a mechanical problem which may indeed be difficult but which, with our present methods of anesthesia, is not impossible.

Operative Technic.—Perhaps only three procedures in the operative treatment of mediastinal tumors require comment. These are: (1) The choice of anesthesia. (2) The thoracic approach to the lesion. (3) The closure of the thoracic wound.

(1) After trying various methods, I have found the intratracheal method of anesthesia uniformly the most satisfactory. It relieves the surgeon of the fear of open pneumothorax; it permits, even, the wide opening of both pleural cavities if this becomes necessary during the course of the removal of the tumor. If the anesthetic is administered by a skilled anesthetist, anesthesia is, generally, smooth and satisfactory. A variety of anesthetic agents may be employed with this method. We have found ether and oxygen very satisfactory; also nitrous oxide-oxygen combined with ether. Most satisfactory of all, I think, is cyclopropane administered through an intratracheal tube; and this has been the anesthetic of choice in recent cases.

(2) The location of the mediastinal tumor determines the thoracic approach. Generally speaking, three operative approaches will be applicable in the majority of lesions. The small to moderately large anterior mediastinal tumors may be approached by an anterior T-shaped incision, the vertical leg of the T being placed parallel with and over an appropriate rib, the horizontal

leg of the T parallel with and over the lateral border of the sternum. A single rib with its costal cartilage is resected subperiosteally. The costal cartilage immediately above and below is divided at its sternal junction. With the pleura opened, and a rib separator properly placed, a large triangular opening is secured, the base at the sternum, the apex at the lateral thoracic wall.

For the upper posterior mediastinal tumors, a posterior approach along the spine with the retraction of the scapula and with the resection of sufficiently long segments of an appropriate number of ribs gives an exposure of the posterior mediastinum sufficiently large to remove all but the very large tumors. For the large tumors which have extended far into one or both pleural cavities, a long incision encircling the hemithorax, with or without the resection of a single rib, is to be preferred.

(3) The importance of the closure of the thoracic wound, after the operation within the thorax has been completed, cannot be overemphasized. Because of physiologic considerations, the closure should be air-tight, so as to prevent the occurrence of a "sucking" pneumothorax, and should be secure, so as to prevent subsequent reopening of the wound. If there has been no soiling during the procedure, closure should be complete and without drainage. Should an effusion occur after operation, this had better be treated by repeated aspirations than by primary drainage in anticipation of its occurrence. If definite soiling has taken place during the operation, the thoracic wound should, nevertheless, be closed completely and drainage, if thought necessary, established by the air-tight suction method at a distance from the wound.

In the immediate postoperative course, the oxygen tent has been found very useful and is regularly employed. The occurrence of an effusion postoperatively is common, and should be recognized early and treated as has been indicated.

It may be of interst to relate our experience at the New York Hospital, with reference to the mediastinal conditions which have been admitted to our medical and surgical wards. This experience demonstrates the great variety of mediastinal conditions which may be encountered in a general hospital, their nature, and, with reference to tumors, our limitations in their treatment. I have added to this number a few cases from my Baltimore and Cincinnati experiences, of which I have accurate records.

An examination of our medical and surgical records shows that, between September, 1932, and November, 1939, 199 patients with diseases of the mediastinum have been admitted to the wards of the New York Hospital. Of this number, 54 cases represent conditions other than tumor, and include five cases of acute mediastinal emphysema, 20 cases of acute or subacute pyogenic mediastinitis, seven cases of tuberculous mediastinitis, 16 cases of tuberculous mediastinal lymphadenitis, and six cases of nontuberculous mediastinal lymphadenitis.

One hundred forty-five of the 199 cases are examples of mediastinal tumor or tumor-like conditions. These may be classified as follows:

(I) Forty-seven were classified as primary malignant disease of the mediastinal lymph nodes. Of these, 29 were diagnosed as Hodgkin's disease and 18 as lymphosarcoma. In about 25 of the cases, the diagnosis was established by biopsy; in the remainder, the diagnosis was made by physical and roentgenologic examination, and the response to roentgenotherapy.

(II) Sixty were classified as primary and secondary malignant disease of the mediastinum. Of these, 31 were diagnosed as malignant disease of the mediastinum secondary to cancer of the lung and the bronchi; and 12 as malignant disease secondary to other malignant conditions. The remaining 17 were primary malignant tumors of the mediastinum and include three cases of superior sulcus tumor (carcinoma), three of liposarcoma, three of neurogenic sarcoma, one of apical fibrosarcoma, five of malignant teratoma, and two of malignant thymoma. The question of surgery arose only in these 17 cases.

(III) Thirty-nine were clasified as benign tumors of the mediastinum. In 17 cases in this group, the diagnosis has not been verified. Of the 22 verified cases, five were diagnosed as dermoid cysts, five chondromata or chondromyxomata, three thymomata, five neurogenic tumors, and one each as a xanthoma, lipoma, glioblastoma and epithelial cyst.

Surgical treatment in the above three groups of mediastinal tumors was considered possible only in the 17 primary malignant tumors in Group (II), and in the benign tumors in Group (III).

An examination of the 17 primary malignant tumors shows that the two malignant thymomata were clearly inoperable. Of the remaining 15 cases, surgical exploration was carried out in 12. In six of the 12 cases subjected to operation, the lesion proved to be inoperable, while in the remaining six cases the tumor was removed. Following operation there were two postoperative deaths, a mortality rate for surgical exploration of 16.6 per cent, and a mortality rate following tumor removal of 33 1/3 per cent. Of the four patients who survived tumor removal, one died about a year after operation from recurrence of the disease, while three are living—two of whom are living more than two years. There are no five-year suryivals in this group so far.

Of the 39 cases diagnosed as benign tumors, operation was performed in 17, and resulted in the removal of the tumor in 16. Following operation there were three postoperative deaths. One death followed removal of a dermoid cyst, one death followed the removal of a large chondromyxoma, and one death followed the removal of a neurofibroma. A fourth death occurred during the infiltration of the thoracic wall with novocain, and before any incision had been made. If this case is excluded, the postoperative mortality in tumor removals is 18.7 per cent. Of the 13 patients who recovered, 12 are living and well. One patient operated upon for a benign chondroma later developed recurrences and metastases from which eventually she died.

SUMMARY AND CONCLUSIONS

A summary of this experience brings out the following points:

(1) In a series of 107 cases of malignant disease of the mediastinum, which includes Hodgkin's disease, lymphosarcoma and primary and secondary carcinoma and sarcoma, only 15, or 14 per cent, could be considered as favorable for surgical treatment. But, if the primary malignant tumors only are considered, surgery appeared possible in 15 of the 17 cases observed and was undertaken in 12 cases. In one-half of these cases it was possible to remove the tumor. The experience suggests that with earlier diagnosis and earlier surgical intervention a greater number of the primary malignant tumors of the mediastinum may come within the field of surgery.

(2) In a series of 39 cases of proven or presumed benign tumors of the mediastinum, a surgical operation was performed in but 17, or 43.5 per cent. In 16 of the 17 cases, the tumor was removed, and of 13 cases which survived operation, 12 are at present well. In one case, operation was abandoned because of the poor condition of the patient. It is of interest to inquire why a higher percentage of supposed benign lesions was not subjected to operation. An examination of the records of the 21 cases not subjected to operation shows that in five, surgical opinion regarding operation was not requested, and the outcome is unknown. Five entered the hospital late in the disease, with advanced symptoms which precluded operation, and died in the hospital or at home. In two, autopsies were obtained and showed neurogenic tumors. Eight patients refused operation. Of these, two have been followed and are now living; one was followed and died at home; two were followed two years, then lost; and three could not be followed. Of the remaining three cases, one was considered too old and feeble for operation, and in two, symptoms were so mild that operation could not be agreed upon. The last two are being followed. In view of the surgical results obtained, it is our opinion that a larger percentage of the benign, or presumably benign, tumors should be subjected to operation.

I am indebted to Doctor DuBois for permission to study the records of patients with mediastinal conditions who have been admitted to the medical wards of the New York Hospital.

HETEROTOPIC PANCREATIC TISSUE PRODUCING PYLORIC OBSTRUCTION

A REVIEW AND CASE REPORT

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UNTIL June, 1939, heterotopic pancreatic tissue has been reported in the literature approximately 340 times. Beaver,[1] in 1933, states that in complete routine autopsies this condition is found more frequently than statistics would indicate.

The majority of these cases have been asymptomatic. The fundamental cause of symptoms has been interference with the normal intestinal motility. Local spasm and muscle hypertrophy and contraction have been characteristic of these lesions in the stomach, duodenum, and upper jejunum; whereas, intussusception has been found entirely in the small bowel where an aberrant pancreas has frequently been associated with diverticula.

Heterotopic pancreatic tissue is of special interest to the surgeon because it may be confused with malignancy and healed or active peptic ulcer. Cross section of the tissue may reveal its identity. Frozen-section at the time of operation reveals its true character.

Statistical Review.—Poppi,[15] in 1935, presented interesting observations based upon 300 cases. The frequency of heterotopic pancreatic tissue was considered (Table I). The anatomic site and frequency of heterotopic pancreatic tissue was reported as follows: Stomach, 31.46 per cent; duodenum, 31.83 per cent; jejunum, 21.7 per cent; ileum, 9.36 per cent; mesentery, *etc.*, 3.37 per cent; biliary tract, 4.49 per cent; spleen, 0.74 per cent. Other sites mentioned in the literature were the umbilicus, appendix, and a dermoid cyst of the mediastinum.

TABLE I

FREQUENCY OF HETEROTOPIC PANCREATIC TISSUE IN CONSECUTIVE AUTOPSIES

Pathologist	No. of Necropsies	No. of Cases Found	Percentage
Feyrter	1,100	25	2.2
Katsurada	329	6	1.8
Kremer	467	6	1.2
Letuelle	180	10	3.0
Mouchet	200	5	2.5
Opie	1,800	10	0.55
Average Percentage			1.875

Etiology.—There are two general theories advanced to explain the occurrence of heterotopic pancreatic tissue. The first, proposed by Zenker[23] and later by Warthin,[21] advances the belief that during the outgrowth of the ventral pancreatic bud, a portion is carried away to its new position by em-

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bryonic tissue development. The second theory, proposed by Taylor,[18] advances the belief that the condition is one of an atavistic tendency, since, in some of the lower animals, the pancreas is normally a divided organ which is found throughout the intestinal tract.

Histology.—In the majority of the reported cases, the heterotopic mass was composed of normal pancreatic cells and a definite duct system which apparently was functioning in a normal manner. Approximately one-third of the cases contained islets of Langerhans. Heterotopic pancreatic tissue has been reported to have been found in varying dimensions, ranging from those of microscopic proportions to that reported by Holzweisig,[12] which measured 6x3.5x1 cm.

The investigations of Delhougne[8] are of practical interest. In the 46 cases that he presented, the site of the heterotopic pancreatic tissue in the bowel wall was as follows: Submucosa, 45.5 per cent; intramuscular, 25.1 per cent; subserosal, 15.1 per cent; and in all of these layers, 14.2 per cent. It is evident that, in approximately 60 per cent of the cases, the mass may be discovered only by careful palpation of the bowel wall.

All pathologic changes that have occurred in the normal gland have been reported in the heterotopic gland tissue. Chronic inflammation has been commonly found. Acute necrosis, malignancy and ulceration have been reported.

Symptoms.—There have been no characteristic symptoms relative to the presence of heterotopic pancreatic tissue. Pain that has localized in the right upper quadrant or in the epigastrium was the most frequent complaint. The medical histories have resembled those of gastroduodenal ulcer, cholecystitis or appendicitis on one hand, and the obstructive signs of pyloric stenosis or intussusception of the intestine on the other. Poppi reviewed 43 such cases and found that in 39.53 per cent a clinical diagnosis of gastroduodenal ulcer had been made.

TABLE II

HETEROTOPIC PANCREAS IN TISSUE CAUSING INTESTINAL SPASM

Author	Reference	Site of Pancreatic Tissue*	Clinical Signs, Diagnosis, Etc.
1. Alessandri	Ann. Stal. di chir., p. 1. 1928.	Duodenum	Cholecystitis
2. Balognesi	Quoted by Poppi.	Duodenum	X-ray: Pyloroduodenal ulcer
3. Cigada, No. 2.	Atti i Mem. Soc. Lomb. di Chir.. 14, 1159. 1934.	Duodenum	Gastric ulcer. Duodenitis
4. Cogniaux, No. 1.	Arch. franco-belges de chir.,	Stomach	Pyloric ulcer
5. Cogniaux, No. 2.	p. 307. 1928.	Duodenum	Pyloric ulcer
6. Gibson	Med. Rec., p. 426. 1912.	Stomach	Emesis. Cholecystitis
7. Gosset, Lowei and Bertrand	Bull. Me n. Soc. de Paris. 8. 860. 1923.	Duodenum	Duodenal ulcer
8. Griep	Med. Klin., p. 877. 1920.	Stomach	Gastric symptoms; X-ray: Hour-glass stomach
9. Gruber	Quoted by Poppi.	Stomach	Emesis
10. Hilarowicz	Zentralbl. f. Chir., p. 1610. 1927.	Stomach	X-ray; Duodenal ulcer
11. Leriche	Lyon Chir., 2, p. 242. 1929.	Diverticulum of stomach	X-ray: Ulcer of pylorus
12. Lesne and Coffin	Bull. Soc. de pediat. de Paris. p. 636. 1925.	Pylorus	Projectile vomiting
13. Letulle and Vinoj	Soc. Anat. Paris. 1921.	Stomach	Gastric symptoms
14. Nova	Atti d. Soc. lomb. di Chir., February, 1933.	Jejunum	Duodenal ulcer syndrome

TABLE II (*Continued*)

Author	Reference	Site of Pancreatic Tissue*	Clinical Signs, Diagnosis, Etc.
15. Pignatti	Atti. Soc. Ital. di Chir., October, 1927.	Jejunum	Duodenal ulcer
16. Pohle	Zentralbl f. Chir., **9**, 1004, 1933.	Duodenum	X-ray: Duodenal ulcer
17. Puhl	Deutsch. Zeitschr. f. Chir., **239**, 624, 1933.	Jejunum	Gastric ulcer
18. Razeman and Vander Dorp	Arch. d. mal. de l'appar. digestif., p. 300, 1931.	Duodenum	Duodenal ulcer
19. Ritter	Bruns' Beitr., p. 157, 1921.	Stomach	Pyloric ulcer
20. Roux-Berger	Bull. Mem. Soc. de Paris, p. 800, 1923.	Duodenum	Duodenopyloric ulcer
21. Schmeiden and Sebening	Arch. f. Klin. Chir., p. 384, 1927.	Duodenum	Duodenal ulcer
22. Tenacerco and Barbillian	Bull. et Mem. Soc. Nat. de Chir., 1932.	Pylorus	Gastric ulcer
23. Wertheimer	Bull. et Mem. Soc. Nat. de Chir., **6**, 1933.	Antrum of stomach	Vomiting; indigestion

* In the above cases no lesion except the heterotopic tissue was found.

Table II presents those cases of Poppi's series which demonstrate symptoms that I have interpreted as having been produced by local spasm of the intestinal wall. In each case the heterotopic tissue alone was found to produce the complaints.

Table III presents all discoverable cases of pyloric stenosis which has been secondary to the presence of heterotopic pancreatic tissue. The obstruction has been the result of muscle hypertrophy and contraction, which resembled

TABLE III

PYLORIC OBSTRUCTION AND HETEROTOPIC PANCREATIC TISSUE

Author	Year Reported	Site of Pancreatic Tissue	X-ray Report	Pathologic and Operative Report
Branch and Gross	1935	Pylorus	Defect of pylorus. 50% residue	1 cm. mass in pylorus
Cecchini, S.	1886	Pylorus	?	Chronic inflammation of pancreatic tissue. Marked hypertrophy of gastric muscle. Compression of pylorus and duodenum
Choisser	1925	Duodenum	?	Hypertrophy of muscle
Cohen	1922	Pylorus	Defect of pylorus. Distended duodenum. 6-hr. residue	Hickory nut-sized tumor; considerable narrowing of lumen; superficial ulceration
Danzis	1938	Duodenum	Pyloric obstruction and duodenal ulcer. 40% residue	Retracted pylorus; tumor 1 cm. in diameter
Delhaugne, F. (1)	1924	Pylorus		Nut-sized tumor; chronic thickening of muscle 1 cm. in size.
(2)		Stomach		in pylorus; hypertrophy muscle
(3)				Hypertrophy of muscle
Gruber, Herle and Roth	1929	Pylorus		Stenosis of pylorus
Gutman and Thalkeimer	1929	Duodenum		Stenosis of pylorus
Hedry	1924			Kronen-sized tumor in anterior wall; infected; hypertrophy of muscle; stenosis, admitting tip of finger
Munch	1924	Pylorus	5½-hr. residue	Benign pyloric stenosis
Raynier and Masson	1909	Pylorus		Nodule size of pea; pyloric stenosis
Simpson	1929	Pylorus	Duodenal spasm	Hypertrophy of muscularis
Thorel	1903			Hypertrophy of muscle
Tschudi, E.	1931	Duodenum	Irregular duodenal bulk: stenosis	Pancreatic tissue in submucosa. Pylorus admits tip of finger
Weishaupt	1917	Duodenum		Pyloric stenosis

that found in cases of long-standing duodenal ulcer, the so-called congenital pyloric stenosis in the infant and adult, and the contracted rectal sphincter. The case herewith reported falls in the group considered in Table III.

Case Report.—Mrs. C. S., white, female, age 45, was referred by Drs. J. L. Siefert and H. Kullman, who had made a diagnosis of pyloric obstruction and cholecystic disease. The patient complained of having had periodic attacks of "gaseous indigestion" for the last 15 years. She had found that certain foods provoked these attacks, and that sodium bicarbonate and the prone position relieved them. The pain had always been crampy in character and had radiated both around the right costal margin and directly through to the back. Vomiting and headaches were occasionally present. At first, these attacks were mild and occurred at long intervals but they gradually became more frequent and more severe. During the previous three months the attacks had been so severe as to confine her to bed for one or two days.

The past history revealed that she had had measles and an attack of "jaundice" during childhood.

Pertinent findings upon examination revealed only obesity and slight epigastric tenderness. Urine was normal. Kline test negative. Hemoglobin, 11.5 Gm.; R.B.C., 3,850,000; W.B.C., 12,000, polymorphonuclears 72 per cent. Blood cholesterol, 286 mg., per 100 cc.; the Graham-Cole dye test revealed a nonfilling gallbladder. The stomach revealed a 40 per cent retention of barium at the end of six hours, but no other demonstrable pathology.

Operation.—June 19, 1937: Exploration revealed the stomach dilated about twice the normal size and hypertrophy of the gastric wall. In the anterior wall of the pylorus, a tumor mass, about 3 Mm. in diameter, projected through the muscularis. This visible mass was the "spearhead" of a button-shaped tumor, about 1.5 cm. in diameter, that could be palpated in the pyloric wall. Through an exploratory incision in the stomach wall, the pylorus could be seen firmly contracted to a diameter of 1 cm.; it could not be dilated. The mucosa opposite the mass had a normal appearance. The gallbladder was normal to inspection and palpation. The appendix was bound down by many adhesions.

The tumor mass and two-thirds of the pyloric sphincter were excised, and a Judd type of pyloroplasty was performed. The appendix was removed.

Pathologic Examination.—Gross: Dr. D. C. Beaver. The specimens consist of a resected portion of the pylorus of the stomach and the appendix. The pylorus reveals hypertrophy of the muscularis, and a definite, firm, nodular zone within the muscularis, which measures 1 cm. in diameter. The mucous membrane is not ulcerated.

Microscopically, the surface epithelium is intact and normal in appearance. The pyloric glands are normal. The superficial portion of the mucous membrane is infiltrated by lymphocytes, which are sometimes organized as lymph follicles. The supporting connective tissue of the mucous membrane is normal in appearance. The muscularis mucosa is normal. The submucosa is normal. The muscularis externa presents marked and uniform hypertrophy of all three layers. The hypertrophy is the result of an increase in size of unit muscular structures and the presence of a large number of ducts and glands. The ducts are lined by columnar, mucus-producing epithelial cells. They vary in size from small to large major ducts, which are usually dilated. The smaller components appear to unite to form the larger ones. Dense connective tissue is present as supporting structure around the ducts. Occasionally lymphocytes are infiltrated in the periductal connective tissue. In the neighborhood of larger ducts, glandular tissue having the histologic characteristics of pancreatic acinar tissue is found (Fig. 1). Islands of Langerhans are not present. At no point do the ducts appear to empty upon the surface in the sections studied. All cells of the ducts and glands are mature and adult in type. The ducts and glandular tissue are present in all parts of the muscularis externa, from submucosa to serosa, but a larger number are found in the middle circular muscular layer.

The myenteric plexus is composed of hypertrophic nerve cells. *Pathologic Diagnosis.*—(1) Heterotopic pancreatic tissue and pancreatic ducts in the wall of the pylorus. (2) Hypertrophy of the muscularis externa of the pylorus. (3) Chronic catarrhal appendicitis.

Convalescence was uneventful. At the present writing, one and one-half years after

FIG. 1.—Photomicrograph of a section through the muscularis externa of the pylorus disclosing multiple ducts of varying size and islands of pancreatic acinar tissue. (H & E stain—×100)

operation, the patient has been free of symptoms, with the exception of minor attacks of duodenal spasm, apparently precipitated by familial discord. Fluoroscopic examination and the clinical course at all other times reveals normal function.

Ritter[16n] has offered two explanations for the spasm of the intestinal muscle in the presence of heterotopic pancreatic tissue. One, an attempt by the musculature to abort a foreign body, and, two, the chemical irritation by pathologic change in the normal composition of the secretion. In my opinion, it would be more logical to believe that the source of irritation was the result of any pathologic change that involved the aberrant tissue.

Table IV presents the cases found in Poppi's series that have concomitant peptic ulcer and heterotopic pancreatic tissue. The first two cases have the ulcer superimposed upon the heterotopic tissue. These cases suggest that the careful surgeon should at least look for heterotopic tissue and consider the removal of any peptic ulcer as a part of the operative technic.

COMMENT.—A review of the material relevant to this subject strongly suggests that constant stimulation of local intestinal musculature by pathologic changes in the aberrant pancreatic tissue have produced chronic contraction

and hypertrophy as an end-result, and that the difference between the cases represented in Tables II and III is that of time and the degree of irritation.

When the surgeon is confronted by normally appearing organs, in a case

TABLE IV

CASES PRESENTING PEPTIC ULCER AND HETEROTOPIC PANCREATIC TISSUE (POPPI)

Author	Site of Pancreatic Tissue	Pathology
Ashanazy	Stomach	Cystic mucosa + duodenal ulcer
Cardwine and Short	Stomach	Acute necrosis of heterotopic pancreatic tissue, with superimposed ulcer
Cave	Duodenum	Duodenal ulcer
Ciceri	Jejunum	Duodenal ulcer
Deaver and Reiman	Duodenum	Superimposed ulcer
Del Valle, Braghetto and Briand	Stomach	Juxtapyloric ulcer causing hypertrophic stenosis
Fumagalli, No. 1	Duodenum	Stellate cicatrix of a pyloric ulcer
Fumagalli, No. 2	Duodenal diverticulum	Cicatrix of a duodenal ulcer
Heinekampf	Duodenum	Duodenal ulcer
Okinczyc, No. 2	Jejunum	Gastric ulcer
Pignatti	Duodenum	Gastric ulcer
Sicca	Stomach	Duodenal ulcer
Sussi, No. 1	Jejunum	Duodenal ulcer
Sussi, No. 2	Stomach	Prepyloric ulcer
Wohlhill	Stomach, fundus	Gastric ulcer
Zanatti	Jejunum	Duodenal ulcer

presenting clinical signs of peptic ulcer, cholecystitis, or appendicitis, a careful visual and palpatory search should be made for heterotopic tissue in the region of the upper gastro-intestinal tract. In the very rare case, an ulcer, may be produced by necrosis of the heterotopic pancreatic tissue. Peptic ulcer and an aberrant pancreas may be found together.

TREATMENT.—The treatment of heterotopic pancreatic tissue is the surgical removal of the mass and the correction of complications that may be present. When pyloric obstruction is present, any applicable technic may be employed to restore the normal gastro-intestinal canal with the exception of the Rammstedt-Fredet procedure.

CONCLUSIONS

(1) Heterotopic pancreatic tissue occurs more frequently than present statistics would seem to indicate, and produces symptoms in only a few cases, but when symptoms are produced they are frequently the result of pathologic changes that are common to the parent gland.

(2) The surgeon should familiarize himself with the gross aspects of this tissue and should resort to frozen-section at the time of operation.

(3) An explanation of the etiology of pyloric obstruction in these cases is offered.

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ILEOJEJUNITIS

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ILEOJEJUNITIS may be defined as the subvariety of regional enteritis in which the granulomatous process typical of that disease extends to involve the upper ileum and the lower or whole of the jejunum.

The original descriptions of regional ileitis concerned the form of ulcerous and hyperplastic inflammation in which the terminal loops of the small intestine, just proximal to the ileocecal valve, are implicated.[1, 2, 3] It was soon recognized that the pathologic process, while presenting its most typical aspect in the terminal ileum, was not restricted to that area; it could and did extend, in a limited number of cases, to the higher loops of small intestine and also, on occasion, transcended the valve to involve the cecum and colon.

It is appropriate to recognize that the clinical picture of upper ileojejunitis is somewhat different from terminal ileitis, bearing its own clinical, pathologic, and roentgenographic characteristics. While allowing it to remain within the category of regional enteritis, upper ileojejunitis has certain clearly recognizable and distinguishable settings.

To contrast the two forms, *terminal ileitis* is marked by a localized granulomatous mass; by numerous external and internal fistulae; by perirectal abscesses; by obstructive intestinal phenomena; and a low-grade febrile clinical course with slowly progressive inanition. The localized process is highly amenable to surgical intervention.

Ileojejunitis is the same ulcerative granulomatous disease extending orally for a variable distance to and including the jejunum, but without the mass, usually without fistulae or rectal complications, without obstructive phenomena. It is, in general, not favorable to surgical help. The course is low-grade, often less severe; a considerable degree of healing under conservative medical therapy is possible, though a complete anatomic restitution to integrity of the bowel is not conceivable.

Etiology.—To date, our experience with regional ileitis or enteritis approximates almost 200 cases. Out of this large number we are able to separate 17 examples of diffuse or high ileojejunitis. The latter serve as the basis for this report. It is immediately obvious that, in comparison with terminal ileitis, ileojejunitis is a less common form, occurring in proportion approximately one to ten of all granulomatous cases.

The age incidence in ileojejunitis is again one of youth, the average age at observation being 25½ years (terminal ileitis 27½ years), the range ex-

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tending from a child of nine years to a maximum seen in a man of 70. Males predominate in the proportion of over two to one, 12 males to five females.

As regards the direct etiology of the disease, no further or new knowledge is available. The process is definitely not tuberculous, either by culture, histology, staining, or by animal inoculation.

In two instances we were able to recover a *Shigella dysenteriae* of the Flexner variety from the stool of the patients, proven by culture, reactions on sugar media, serum agglutinations, and absorptive phenomena carried out on the cultures.

Ileitis as a disease may be a clinical variety of dysentery, or at least at its initiation it may originate as a dysentery infection. If so, then the difficulties in discovering and recovering viable dysentery organisms from the stools of chronic cases is obvious to anyone familiar with the bacteriologic aspects of epidemic dysentery. In a recent endemic of typical dysentery in the personnel of the Training School for Nursing, of the Mt. Sinai Hospital, during the summer of 1939, over 250 cases were observed and studied. Positive dysentery cultures of the Newcastle strain were recovered in a large percentage of the cases (79.4 per cent), but only in the first one to three days of the onset; after that initial period, cultures of the stools were almost uniformly negative.

If ileitis is dysenteric in nature, then the difficulty of obtaining cultures in cases which have already run a course of from one to 14 years, before coming under observation, is self-evident. The ability to recover, in two of the 17 cases of ileojejunitis, viable Flexner organisms, is certainly striking. Again, one of the cases seen was a younger brother of one of the 14 original cases[1] of terminal ileitis. The brothers had lived together for some time, and the possibility of a transfer infection, through food handling and careless toilet hygiene must be considered. This latter instance is now one of five examples of ileitis in siblings, among whom, two, and in one instance, three members of the same family were affected.

On the other hand, to date, as far as we know, none of the 250 nurses, involved in the hospital epidemic of 1939, have developed any sequelae or evidence of any chronic symptoms of the malady, either as chronic colitis or as ileitis.

Pathology.—The pathology of ileojejunitis varies only slightly from that of regional ileitis. It is a granulomatous and ulcerating, nonspecific inflammation, in which all of the coats of the intestinal wall, particularly the submucosa, undergo a granulomatous, proliferative change. The overlying mucosa undergoes a process of linear necrosis, paralleling the extension of the ulcerative process. Miliary-like tubercles consisting of lymphoid and epithelioid mononuclear cells are common and frequently enclose giant cells, probably of foreign-body nature.

Grossly, dense mass formation in ileojejunitis is unusual, nor does the process concentrate on any one area to produce a large granuloma with encroachment upon the lumen of intestine, as is seen in terminal ileitis. The

process is more diffuse, a large part of the small intestine is usually involved (except for the duodenum) by numerous "skip-areas," separated by large-spaced distances of free mucosa. The process does not reside in one place long enough to create obstruction to the lumen or to originate fistulous tracts; instead, the disease seems to disseminate its power, continually advancing upward by kangaroo-like jumps to involve higher intestinal segments (Chart 1). Enlarged mesenteric lymph nodes accompany the extension of the dis-

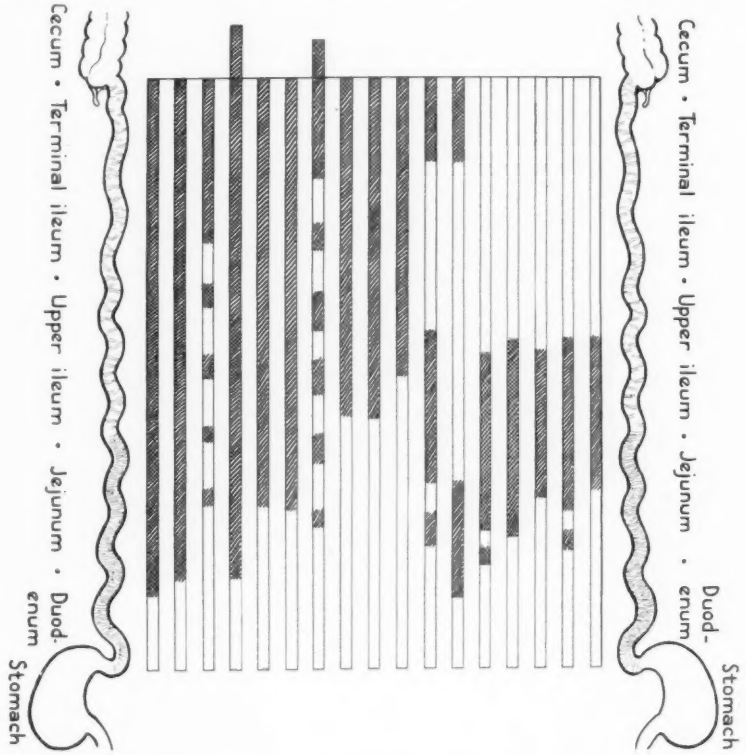
Cecum • Terminal ileum • Upper ileum • Jejunum • Duod-enum
Stomach
Cecum • Terminal ileum • Upper ileum • Jejunum • Duod-enum
Stomach

CHART 1.—Demonstrating, graphically, the anatomic distribution of the lesions in diffuse or high ileojejunitis. (Shaded areas denote the extent and location of the pathologic involvement.)

ease, though the nodes in the mesentery of the upper ileum and jejunum rarely achieve the massive and succulent proportions seen in the mesentery just proximal to the ileocecal valve. Whether the extension of the malady to new intestinal areas is achieved by mucosal transport or by invasion of the lymphatics is still controversial.

In only two cases were fistulous tracts observed; in one, an ileorectal fistula, in another, an ileo-ileal fistula occurred. External fistulae to the abdominal wall were not observed, even though the recent scars of an exploratory celiotomy existed in five cases (in contrast to regional or terminal ileitis).

Symptomatology.—The onset is usually gradual (15 cases), the duration

of the symptoms, when first seen, being from six months to 14 years (average, three and one-half years). Only two cases presented an, apparently, acute onset: one, with gross hemorrhage, the other, with an acute febrile course. Both cases, when seen, were, however, already well-advanced in the chronic phases of the disease. Four patients had previously undergone an ineffectual appendicectomy.

The outstanding symptoms in all cases were: (1) A low-grade febrile course. (2) Abdominal pain, often amounting to severe cramps. (3) Diarrhea. (4) Gross hemorrhage. (5) Anorexia. (6) Marked loss of weight.

The temperature remained within normal range in six instances, and was elevated to 100° to 104° F. in the remaining 11 cases. The fever was irregular in nature, sustained often for several days or weeks, or alternating with periods of apyrexia.

Abdominal pain and cramps were universally present—diffuse, moderate at times, severe at others; ranging over the lower abdominal segments and periumbilical region. Paroxysms of severe cramp-like pain were common in both lower right and lower left iliac quadrants, usually followed by a diarrheal movement. With the passage of the fluid feces and gas, accompanied by an audible gurgling, the cramp was allayed. At times, the paroxysms called to mind low-grade intestinal obstruction, though none of the 17 cases ever came to operation because of suspected obstruction.

Diarrhea was universally present, two to four or six stools per 24 hours. This diarrhea is less severe than is seen in ulcerative colitis; the stools are mushy, or semisolid, and when more frequent, actually watery, containing mucus, but no pus, and only occasionally blood. At times, constipation alternated with diarrhea. It is of interest that the guaiac reaction in the feces was positive in ten cases, but persistently negative in five cases. Gross hemorrhage was present in three patients, in one, as the initial symptom.

Anorexia was a common manifestation, particularly in the febrile cases, and was associated in all instances with a marked loss of weight. The average weight loss amounted to 17½ pounds, the extremes ranging from four to 40 pounds. During the healing phases, after the initial stages of severity have passed, actual gains of 15 to 25 pounds of body weight have been observed.

Nutrition is usually poor, the skin dry, the mucous membrane pallid. An aphthous stomatitis was observed twice, and in one of these patients recurrent aphthous ulcers were accompanied by bleeding gums. Except for these manifestations of hypovitaminosis no striking clinical changes characteristic of vitamin deficiency were observed.

The degree of anemia was not marked; in one case, a low of 50 per cent was reached, but many patients preserved a hemoglobin ranging between 75 and 94 per cent. One patient had a macrocytic hyperchromic type of anemia, with a color index of 1.3. This individual had been treated as a case of sprue until a gastro-intestinal roentgenologic study showed the characteristic changes of ileojejunitis; interestingly enough, and in contrast with sprue,

the macrocytic anemia improved only slightly with daily injections of liver extract—a maximum reticulocyte response of only 7 per cent being attained. The remaining patients with anemias presented blood pictures of the microcytic hypochromic variety.

The leukocyte count in ileojejunitis was usually within normal limits, the highest (which was most unusual) being in one instance 12,900, and in another, 18,000 cells. The differential count was noteworthy of deviation from the norm in that a relative or absolute eosinophilia was present in five patients, the highest content being 14 per cent.

Oral glucose tolerance tests were performed on seven patients, and in five, flat curves consistent with poor absorption were obtained. The erythrocytic sedimentation rate exhibited varying degrees of acceleration in five patients (22 to 50 minutes—normal being 60 minutes or more). Sedimentation rates were increased in three of Snapper's[6] six cases of chronic ileitis. The total protein in the blood plasma was appreciably lowered (5.8 Gm.); in three cases, reaching a minimum of 4.0, 4.4 and 4.5 Gm. per 100 cc.; the albumin-globulin ratio was persistently disturbed, approaching a ratio of one, but never completely reversed. The urea, blood sugar, and phosphorus in the blood plasma were within normal ranges. The blood calcium was reduced in one patient; another patient showed an osteoporosis of the pelvis, thought to be due to loss of calcium in the stool. Improvement was noted following calcium therapy. Gastric analysis showed normal acidity titers in all cases except in one instance in which a true achylia was present.

Tuberculin reactions (Mantoux and von Pirquet) were negative. Dysentery agglutinations for B. Flexner, Hiss, Shiga, Mt. Desert, and Sonne were negative in eight patients, and the blood Wassermann reaction was negative in all. Roentgenograms of the lungs in many cases were entirely negative.

The Physical Examination.—The physical examination of the patient, apart from malnutrition and pallor, evidenced tenderness over the entire abdomen, frequently more marked in the lower segments. A mass was never felt, nor were external abdominal wall fistulae observed. Visible peristalsis was not present. The edge of the spleen was occasionally palpable, soft and sharp.

The rectal examination was always negative, this again contrasting with terminal or regional ileitis in which a pelvic mass or induration is frequently palpable and corresponds to an involved localized granuloma with localized peritonitis and diffused fistulous tracts. Sigmoidoscopy was always negative.

Roentgenologic Studies.—The diagnosis of ileojejunitis, being marked by the lack of physical signs, rests mainly on roentgenographic evidence. The barium enema is usually the first procedure, for in every case of persistent diarrhea, the primary interest rests in recognizing or excluding an ulcerative colitis. A negative sigmoidoscopy does not exclude the possibility of a right-sided segmental colitis, the evidence of which is clearly demonstrable following a barium clysma.

In most cases of ileojejunitis the opaque enema is negative (15 out of 17

observations). In one instance a persistent cecal spasm, in another, definite spasm and deformity of outline in the transverse and descending colon gave warning of colonic participation in the process; this was confirmed at celiotomy.

The eventual diagnostic procedure was, and is, the barium meal, as performed with a reduced amount of barium (four ounces or less), and with frequent fluoroscopic observations and roentgenograms. When properly carried out, the roentgenographic demonstration of the disease is, and should be, a relatively simple task.

By roentgenologic studies following a barium meal, the degree and extent of ileal and jejunal involvement are definable with a good degree of accuracy. The lower jejunum and upper ileum were always seen to be involved; in five instances, the terminal ileum seemed to be exempt from the process. In two cases, six to seven inches of terminal ileitis was followed by a long free area, the distal half of the ileum and the lower jejunum being again the seat of an advanced pathologic process. Occasionally, clearly marked "skip-areas" were easily demonstrated in the roentgenograms.

Ten of the 17 cases have been subjected to exploratory celiotomy, in all of which the roentgenographic diagnosis of the disease, as well as the extent and degree of invasion, were amply and accurately confirmed.

Differential Diagnosis.—In terminal ileitis it is important to exclude primary and secondary tuberculosis and neoplasm, both of which are marked by extremely severe courses and are readily differentiated roentgenologically and by laboratory examinations.

With upper ileojejunitis, an entirely dissimilar problem comes into play. Here, benign new growths are uncommon, but Hodgkin's disease and sarcomatosis occur and are characterized by rapidly downhill course with hemorrhage and emaciation.

The main point in high ileojejunitis is to exclude nontropical sprue, and the intestinal manifestations of the deficiency diseases. Clinically, nontropical sprue is characterized by frequent, frothy stools, and by the finding of a severe anemia, frequently of the hyperchromic type. Fever is absent, the stools do not contain blood, and gross hemorrhage from the bowel is absent. The cases react well to liver extract, to careful and judicious dieting, and to hygienic measures. The roentgenographic picture of the small bowel in sprue is one of uneven distribution of the barium in the several loops of the jejunum and ileum, with delay in motility of the upper loops, and without changes in the terminal ileum.[7, 8]

It is necessary to differentiate ileojejunitis from the deficiency states and the disturbances of fat metabolism as described by Snell and Camp,[9] Kantor,[10] and by others. The small intestinal changes accompanying ulcerative colitis which have been described by Mackie and Pound,[11] are probably also deficiency states. The roentgenograms in both conditions are of a nature similar to that described in sprue, namely, mild puddling, delay and irregular outlines of the upper jejunum and ileal loops, absence of delay in the terminal ileum.

In true ileojejunitis of the granulomatous type, the whole small intestine including the lower and terminal ileum, is usually involved; but even when only isolated segments of upper ileum and jejunum are implicated, the roentgenographic appearance is quite characteristic. Prolonged delay and accumulations of barium in upper loops is unusual; the various involved segments are irregular and fuzzy in outline; areas of narrowing in the lumen (signifying involvement) alternating with areas of dilatation ("skip-areas") usually increase in severity as one travels distally and is most marked in the

FIG. 1.—Roentgenogram showing the change in outline and in the mucosal pattern in the upper ileum and lower jejunum.

FIG. 2.—Roentgenogram showing the almost continuous "string-sign" involving the whole of the lower and upper ileum.

terminal loops of ileum where the pathognomonic "string-sign" just proximal to the ileocecal valve is frequently observed (Figs. 2 and 3).

Course and Prognosis.—The progress of a case of ileojejunitis depends, to a considerable degree, upon the severity and extent of the disease and the amount of involvement of the small bowel. In those instances in which the greatest part of the small intestine is continuously or intermittently continuously involved, surgical treatment is logically out of the question. To resect the whole implicated area, leaving only the jejunum and duodenum to assume the vital functions of chymification and absorption is to invite disaster. To attempt a high short-circuiting operation, of jejunum to colon, is tantamount to a total exclusion of the small intestine, and is again representative of poor surgical judgment. In those widely diffuse cases, medical treatment, whatever that implies, is the only resort, and is apparently, from a study of conservatively treated cases, most promising.

Nine such cases which have been observed during the last five years have not had recourse to surgical treatment. Four have done very well, having gained strength and weight, in one instance, up to 50 pounds.

The remaining five conservatively treated cases, have gained some weight, anemia has diminished and the frequent bowel movements have decreased and been held under control. The treatment instituted has consisted of a strict nonroughage diet, very liberal vitamin therapy, the administration of iron and liver extract particularly by mouth, and the insistence on rest, sunshine and change of air. The fecal movements are controlled, where necessary, by very small doses of opium after alternate defecations. No specific form of therapy can be evolved in the absence of knowledge of the specific causative agency of the disease. Roentgenotherapy has proven useless, as have also occasional recent attempts at chemotherapy with the newer sulfanilamide compounds.

FIG. 3.—Roentgenogram showing the extent of the diffuse ileitis when first seen.

FIG. 4.—Roentgenogram of the same case as shown in Figure 3, three years later, after a gain of approximately 30 pounds. Note the partial restoration of the width of the intestinal lumen and mucosal pattern.

Clinical and symptomatic improvement takes hold gradually and seems to gain momentum as the years progress. In all the cases in which careful follow-up roentgenologic studies have been made, the observations continue to show the characteristic small bowel changes as originally seen at the first examinations (Figs. 3 and 4). This fact is most significant; two cases have been continually observed for five years; each case has gained from 30 to 50 pounds and is apparently quite well except for mild persistent diarrhea.

Where the disease begins before or at puberty a considerable retardation

of secondary sexual development takes place. One boy was 18 years old, weighed 81 pounds, had infantile testicular development, and was devoid of pubic or axillary hair. His voice was high-pitched and effeminate. (Case quoted by courtesy of Dr. John Sproul of Haverill, Mass.) The second boy, who has done very well on medical therapy, has permanently overcome his developmental sexual retardation, and with the subsidence of active symptoms has finally gained considerable weight, grown to normal stature, and has shown secondary sexual development.

Results and Nature of Surgical Intervention.—Apart from exploratory operations, and the usually needless appendicectomy, a study of the attempts to approach this problem by radical surgical procedures is most interesting. Two cases had undergone wide and extensive resections of the lower bowel and cecum, including all of the ileum, and in one instance, much of the jejunum. The former case survived (Dr. A. A. Berg), and eventually gained 20 pounds in weight, but of late has lapsed, with the development of a diffuse colitis. The latter, and still more extensive resection, died of exhaustion and shock during his immediate postoperative course. Obviously, radical excision of the small intestine, in most of its entirety, is not to be recommended. In a third case, a high jejunocolostomy had been ill-advisedly performed elsewhere. An attempt to revise the operation and to stay the rapidly downhill course by taking down the anastomosis, resulted in a fatal peritonitis. In still another case, a man, age 71, with a course suggestive of neoplasm, a resection of 45 cm. of ileum was performed, though a more diffuse involvement was recognized at the time. This procedure also resulted fatally, and, at autopsy, the whole small bowel was seen to be almost continuously involved in the granulomatous ulcerative process. The operation was forced by the internists because of the obviously hopeless issue under conservative management.

These four cases (with only one survivor) demonstrate the futility of attempting to resect and excise so extensive a disease process.

Attempts at partial resection where the disease is not continuous, or where the distal ileum is exempt and only segmental high ileojejunitis exists, may possibly give more promising results. In two of the cases of restricted, high ileojejunitis, localized resections were performed involving in one case, 90 cm., in the other case, 75 cm. of upper ileum and lower jejunum. In the former case (case of Doctor Sproul), subsequent roentgenologic studies showed residual disease in the small bowel; at a subsequent celiotomy, it was obvious that the entire ileum and jejunum were markedly thickened, edematous, with roughened serosal surface, and a plastic peritoneal exudate. The colon appeared normal. Considerable later clinical improvement has taken place, but this betterment may well be attributed to the meticulous hygienic and conservative treatment instituted since the attempts at reconstructive surgery.

The second case of localized ileojejunal resection is too recent to allow

of any conclusion, although the patient is rapidly gaining weight, and is completely free of symptoms.

What shall or what can the surgeon do who opens the abdomen of a patient and finds a diffuse ileojejunitis involving not only in a severe degree the terminal ileum, but by continuous "skip-areas" the whole extent of the small bowel practically up to the duodenum? To close the abdomen without making some attempt at resection appeared in these remaining two cases as a surrender without an effort at some type of reconstructive surgery. In both instances, the downward preoperative clinical course and the progressive loss of weight and inanition marked the ineffectiveness of conservative attempts at therapy. In this extremity, both redoubtable and experienced surgeons decided upon the same procedure, namely, to resect the most advanced lesion in the ileocecal area (terminal ileum and ascending colon), with the performance of a transverse ileocolostomy. In both instances (Dr. A. A. Berg and Dr. J. W. Hinton) the obviously diseased upper ileum and jejunum were returned to the abdomen. Both patients made uneventful operative recoveries, and, remarkable to say, have apparently continued to show marked improvement (six and three months postoperative).

The improvement in these last two cases is real and cannot be doubted, though it is against all our experiences regarding the success or failure of surgery in regional ileitis. The 10–15 per cent of conceded recurrences following resection for regional ileitis are actually attributed to the fact that higher "skip-areas" have been overlooked at the time of operation. If that be the case, then any palliative and partial resections, such as these latter two, in which no attempt was made to include the higher diseased area, should have been total failures. One would expect to see a rapidly continued downhill course. Not so, however, for the postoperative course has been and continues to be most promising. How to explain such a deviation from the rule is most difficult.

Until medical science reveals how ileitis spreads, whether by mucosal transport or by lymphatic extension; until the cause of recurrences after resection shall have been adequately demonstrated, and the significance of "skip-areas" made clear, the explanation of clinical postoperative betterment in these two unusual cases will remain enigmatic.

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NEPHRO-OMENTOPEXY AND NEPHROMYOPEXY IN THE TREATMENT OF ARTERIAL HYPERTENSION*

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THE PROBLEM of increased arterial blood pressure has assumed vast importance in recent years. As a cause of death, it is preeminent since, directly or indirectly, hypertension causes four times as many deaths as does cancer; moreover, its victims fall into a lower age-group than do those of malignant disease. The resistance of hypertension to effective medical treatment has attracted the surgeon to the problem and his attack has centered particularly upon the nervous system (splanchnic resection, anterior nerve root section, *etc.*), the objective being the elimination of vasomotor stimuli to the vascular tree. In general, the results of these operations have not been up to expectations.

The classic work of Goldblatt and his associates[1] on the production of hypertension in animals (dogs and monkeys) by constricting the main renal arteries stimulated the present studies. These workers found that constriction of only one renal artery was followed by hypertension lasting for days or weeks, the blood pressure eventually returning to the normal level; chronic persistent hypertension could be produced only by constricting both main renal arteries (bilateral renal ischemia) or by constricting the main renal artery of one kidney and removing the other kidney. They observed that in animals with experimental hypertension, whenever the blood pressure fell to a lower value it was due either to inadequate clamping of the renal arteries or to the development of an adequate collateral circulation by the kidney through the ureteral and capsular vessels.

It follows naturally that if human essential hypertension is the counterpart of hypertension produced in animals by renal ischemia, an adequate collateral circulation brought to one or both kidneys would be followed by a return of the blood pressure to lower levels. However, there is a fundamental difference between the two forms of hypertension. In human essential hypertension renal ischemia is rarely due to obstruction of the main renal arteries (such cases, however, have been described) but to a diffuse narrowing of the preglomerular arterioles. It seemed important, nevertheless, to determine whether an improvement of the vascular supply to the human kidney by increasing the accessory circulation would result in a fall in blood pressure

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in patients with arterial hypertension. As will be described in detail later, this has been accomplished by approaching the kidney through the abdominal route, decapsulating the organ, and finally enveloping it in a new fatty capsule of omentum (nephro-omentopexy) or by placing the decapsulated organ in contact with the surfaces of the quadratus lumborum and psoas muscles (nephromyopexy).

Clinical and Experimental Basis for the Present Operative Approach.—The extent to which the omentum will supply blood to ischemic tissue in humans is well exemplified by the increase in the caliber of the omental vessels when this organ becomes attached to pedunculated uterine fibroids and uterine sarcomata. In dogs, Beck[2] and O'Shaughnessy[3] have shown that the grafting of skeletal muscle or omentum to the myocardium rendered ischemic by ligation of one or more of the coronary arteries is followed by increased vascularization of the heart. Approximately ten years ago, Pauntz,[4] and more recently, Davis and Tullis,[5] and MacNider and Donnelly[6] have demonstrated that an accessory blood supply to the normal kidney of the dog may be obtained by nephro-omentopexy. In these investigations, the kidney was prepared by introducing omentum into the incised cortex of the kidney. This procedure was avoided in the present operative approach in patients since it was believed that more scar tissue would be formed between omentum and kidney than when two normal surfaces are placed in apposition. In a previous report, it was shown that under these latter circumstances little or no scar tissue resulted from nephro-omentopexy in humans; at the same time it was demonstrated that communication between the omental and renal blood vessels occurred.[7]

Operative Procedure.—The anterior transperitoneal approach has proved adequate for the preparation of both kidney and omentum for nephro-omentopexy. The stages of the operation have been worked out on succeeding cases. In the first attempt, the operation was performed by the same approach, the arrangement of the omentum and the placement of the kidney being similar to the method in use at present. To this has now been added (a) the removal of a biopsy specimen of kidney substance performed by cutting out a wedge-shaped section of kidney cortex and by placing a mattress suture through the cortex to control bleeding; (b) brain clips have been clamped into the margin of the omentum at each suture point in order to later identify the omental position in relation to the kidney pelvis after an intravenous urogram; and (c) the surface of the kidney has been seared with a cautery, the assumption being that a light searing of the surface will cause an immediate active hyperemia.

The operative procedure (nephro-omentopexy) is relatively simple, requiring from 30 to 50 minutes to perform. The technic is illustrated in Figures 1 to 4, and described in their legends. The technic for nephromyopexy does not require entering the abdominal cavity. The usual lateral oblique incision in the flank is used to reach the retroperitoneal space. The kidney is stripped of its fatty capsule and delivered into the incision in the

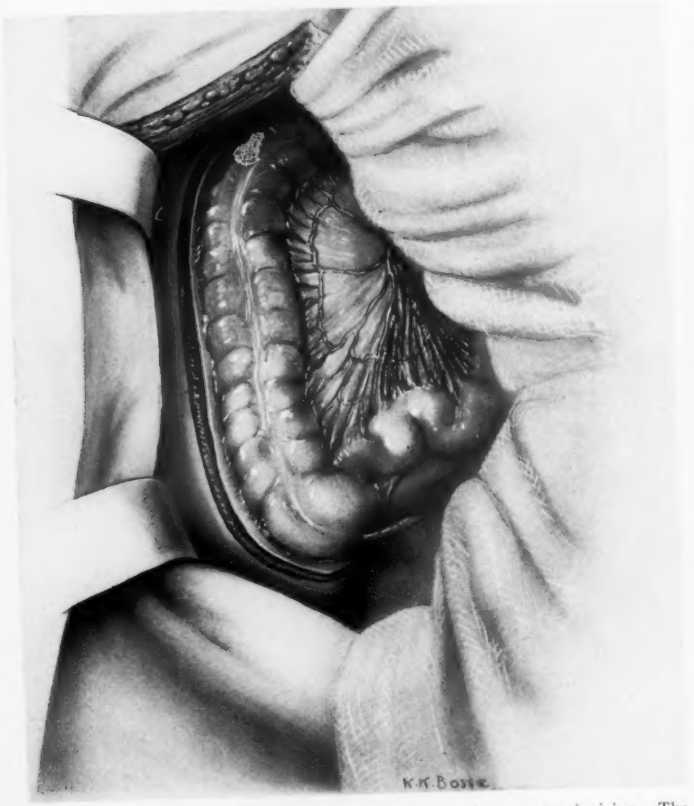

FIG. 1.—The approach is through a long external pararectus incision. The small intestines are packed off to the left of the abdomen. The upper abdominal peritoneum is incised externally to the ascending colon and cecum. In one instance (Case 6) this lateral incision was carried up to the level of the first portion of the duodenum; this was necessitated by an extremely short omentum.

FIG. 2.—The cecum and ascending colon are lifted away from the posterior abdominal wall. The kidney is freed from its fatty capsule by blunt dissection and delivered into the abdominal cavity. The true capsule of the kidney is divided along the convex border; the medial half of the capsule is removed close to the pelvis.

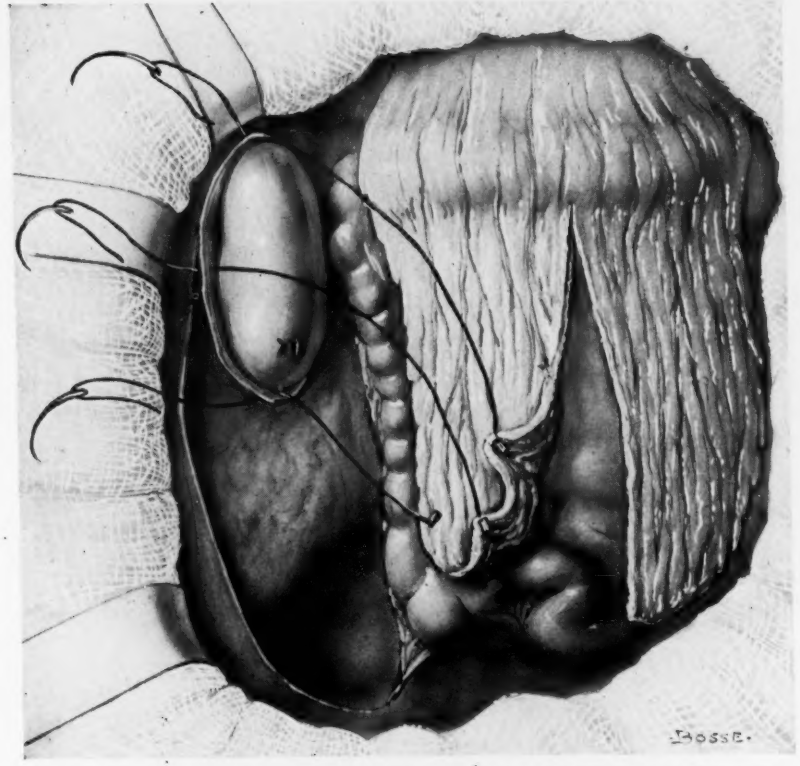

FIG. 3.—The lateral half of the kidney capsule is divided near the kidney pelvis leaving a sufficient margin to suture to the omentum. The omentum is divided in the midline, care being taken to avoid cutting any of the large vessels. Removal of a biopsy specimen of the kidney is now taken, usually on the convex surface near the lower pole. Superficial searing of the kidney surface is then carried out. Brain clips are clamped into each corner and into the middle of the lower margin of the omentum. Leading sutures are taken from each corner of the omentum and from its lower midborder to each pole of the kidney and to the midline of the posterior cut margin of the capsule. As the sutures are drawn up, the omentum is pulled upward and laterally to cover the convex and posterior surfaces of the kidney. The kidney is then rotated and replaced in its normal position.

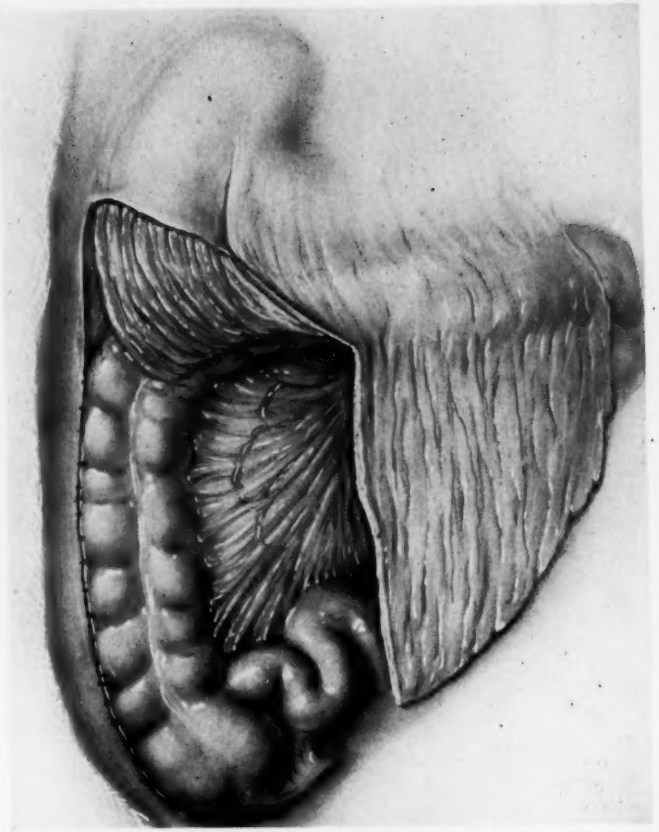

FIG. 4.—The replacement of the kidney in the retroperitoneal space drags the omentum with it through the superior angle of the incision in the posterior parietal peritoneum. The anterior surface of the kidney is covered in this way. The lateral incision into the posterior abdominal peritoneum is then closed up to where the omentum leaves the abdominal cavity.

usual manner. The true capsule is incised along the convex border of the kidney, stripped back and removed from the anterior surface of the kidney. On the posterior surface the capsule is divided along the pelvic border with enough margin left to suture to the left margin of the psoas muscle in order to support the kidney. The lumbodorsal fascia is removed from the quadratus lumborum and psoas muscles directly posterior to the kidney. In Case 7 the lower pole of the kidney could be slipped into the lumbodorsal fascia which served as an additional means of supporting the kidney (Fig. 5). As in the

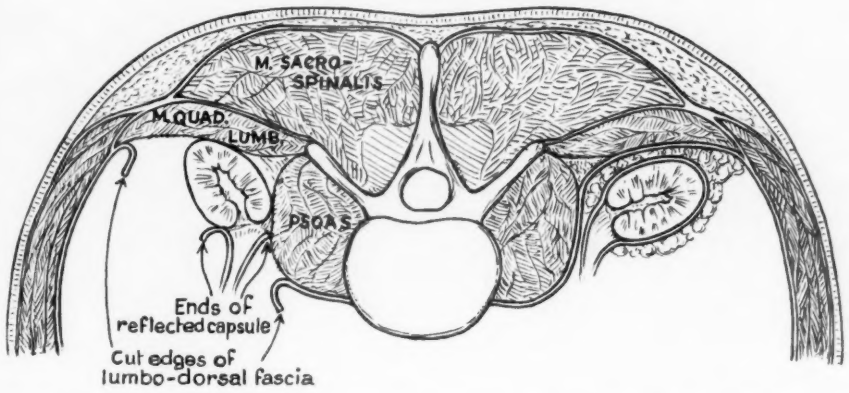

FIG. 5.—Relative position of the kidney and the surrounding muscular structure in nephromyopexy.

nephro-omentopexy, a biopsy specimen of the kidney is obtained, a brain clip inserted over this area, and the kidney surface seared prior to its apposition to the muscles.

Selection and Preoperative Investigation of Patients.—Each patient was hospitalized for 10 to 30 days prior to operation and a complete clinical and laboratory investigation carried out. This consisted of history and physical examination including eyeground studies, electrocardiogram, blood chemistry, urea clearance and other tests of kidney function, urine analyses and urine cultures, intravenous urogram and, where indicated, retrograde pyelograms. Blood pressures were taken at least once daily. Cases 5 to 9 were selected because of the lability of the blood pressure as shown by the degree of fall after sodium amytal (Allen and Adson[8]) and by the inordinate rise of the blood pressure after immersion of one hand in ice water (Hines and Brown[9]).

Since August, 1937, when the first operation of this type was attempted, six patients have had a right nephro-omentopexy, two a right nephro-omentopexy and six months later a left nephromyopexy, and one a right nephrectomy (for lithiasis and pyelonephritis) and four months later a left nephromyopexy. Two of the patients had nephritis. One of these (chronic diffuse glomerular nephritis) was operated upon not with a view to prolonging life but to determine whether the blood pressure would decrease following such an operative interference and if so to offset the rapidly advancing retinopathy. The other was diagnosed as malignant nephrosclerosis but a

biopsy specimen of the kidney revealed an acute fulminating extracapillary glomerular nephritis. This was confirmed at necropsy. Seven were patients with essential hypertension with the possible exception of one in whom the biopsy specimen removed from the right kidney was strongly suggestive of pyelonephritis.

Postoperative Course.—The immediate postoperative period following the two types of kidney operations described varied in the different patients. In those with little or no kidney damage, recovery from the operation was uneventful. In two patients with relatively severe kidney lesions, there was marked postoperative distention, nausea and vomiting. Wound dehiscence took place in one instance. No pulmonary or cardiac complications were observed in spite of the use of general anesthesia (this form of anesthesia was employed because of the increased apprehension usually exhibited by these patients). There has been no fatality in the immediate postoperative period.

Clinical Observations.—Tables I to IV show the results obtained in the nine patients. The preoperative and postoperative clinical status, and the postoperative blood pressures, are included in these protocols.

Effect upon the Heart.—The operative procedures described exerted no deleterious effect on the heart as determined by clinical and electrocardiographic studies.

TABLE I

NEPHRITIS—RIGHT NEPHRO-OMENTOPEXY

Case	No. 1	No. 2
Age and sex	38; M.	30; M.
Clinical diagnosis	Chronic diffuse glomerular nephritis	Malignant hypertension
Duration of hypertension	2 years	9 months
Preoperative status		
Heart (EKG)	Not done	Normal
Kidney function	Urea clearance 30 per cent of average normal	Urea clearance 12 per cent of average normal
Kidney biopsy	Not taken	Acute diffuse extracapillary glomerular nephritis (subacute nephritis)
Fundus	Severe retinopathy	Severe retinopathy
Blood pressure (Av. 10 days preop.)	226/164	194/124
Postoperative blood pressure		
1 week	206/145	186/126
2 weeks	208/151	178/108
1 month	150/118	
Postoperative clinical status		
Subjective	Marked improvement first month postoperative	No change
Objective	Improved visual acuity. Impairment in renal function not increased	Advancing renal insufficiency
Remarks	Died approximately 1½ mos. postoperative during attack of acute paranoia. Actual cause of death not known.	Died approximately 2 wks. postoperative of retention urêmia

Effect upon the Blood Pressure.—In patients with essential hypertension, unilateral (right) nephro-omentopexy was followed frequently by an appreciable fall in blood pressure for two to three months after the operation

(Cases 3, 4, 5 and 8, Table II; and Case 6, Table III) but within six months the blood pressure usually returned to the preoperative level. In one of the two patients with nephritis, a pronounced fall in blood pressure occurred for one month following unilateral nephro-omentopexy. This patient died one and one-half months postoperative, in a private sanitarium during an attack of acute paranoia; the exact cause of death was unknown (Case 1, Table I). Only two months have elapsed since the bilateral operations were carried out (Cases 6 and 7, Table III; and Case 9, Table IV). Obviously, insufficient time has elapsed to determine their effect, if any, on blood pressure.

TABLE II

ESSENTIAL HYPERTENSION—RIGHT NEPHRO-OMENTOPEXY

Case	No. 3	No. 4	No. 5	No. 8
Age and sex	51; M.	38; M.	44; F.	35; F.
Duration of hypertension	5 yrs.	6 yrs.	10 yrs.	3 yrs.
Preoperative status				
Heart (EKG)	T changes	Normal	T changes	Not taken
Kidney function	Normal	Normal	Normal	Normal
Intravenous urogram	Negative	Congenital anomaly right renal pelvis	Imperfect filling of right calices (pyelogram negative)	Negative
Kidney biopsy	Benign nephrosclerosis	Apparently normal	Strongly suggestive of pyelonephritis	Benign nephrosclerosis
Fundus	Moderately severe retinopathy	Mild retinopathy	Mild retinopathy	Minimal retinopathy
Blood pressure (Av. 10 days preop.)	232/144	192/123	200/116	202/122
Postoperative blood pressure				
1 mo.	198/118	202/142	158/102	
2 mos.	218/131	219/158	172/112	190/130
3 mos.	240/146		213/134	240/140
4 mos.	238/146		156/108	240/160
6 mos.			156/98	
7 mos.	250/130		230/124	
10 mos.	250/130		186/122	
11 mos.			192/118	
Postoperative clinical status				
Subjective	No improvement	No improvement	Moderate improvement. Vertigo and headaches have disappeared	Gained weight felt less irritable for 2 mos. postop.
Objective	Progressive mental deterioration	Attacks of acute abdominal pain	Decided improvement in eyegrounds	
Remarks	Eviscerated 14 days postop. Not known if omentum in apposition to kidney. Died in mental disease hospital 13 mos. postop.	Died 2½ mos. postop. from ruptured aneurysm of celiac axis.		Irritability, nervousness and headaches have now returned

Effect upon Renal Function.—Nephro-omentopexy and nephromyopexy were not followed by any measurable impairment in kidney function of a permanent nature. Occasionally, the urea clearance fell considerably in the immediate postoperative period; the return to the preoperative level, however,

was usually prompt. No evidence of improved renal efficiency was observed nor did these operations inhibit advancing renal insufficiency (Case 2, Table I; and Case 7, Table III).

Effect upon the Ocular Fundi.—Of interest was the report of the ophthalmologist (Dr. Martin Cohen) who believed two patients with essential hypertension presented less evidence of vascular damage in the fundi approximately three to four months after unilateral nephro-omentopexy (Case 5, Table II; and Case 6, Table III). In one patient, benign arteriolar sclerosis of the retinal vessels progressed to a severe retinopathy including papilledema, hemorrhages and exudates six months after right nephro-omentopexy (Case 7, Table III).

TABLE III

ESSENTIAL HYPERTENSION—RIGHT NEPHRO-OMENTOPEXY AND LEFT NEPHROMYOPEXY

Case	No. 6	No. 7
Age and sex	24; F.	48; M.
Duration of hypertension	2 yrs.	10 yrs.
Status prior to right nephro-omentopexy		
Heart (EKG)	Normal	T changes
Kidney function	Normal	Normal
Intravenous urogram	Not definitely abnormal. Pyelogram negative	Negative
Kidney biopsy (right)	Normal	Benign nephrosclerosis
Fundus	Mild retinopathy	Mild retinopathy
Blood pressure (av. 10 days preop.)	186/138	220/130
Blood pressure after right nephro-omentopexy		
1 mo.	150/108	225/130
2 mos.	164/114	
3 mos.	182/134	187/122
4 mos.	186/132	
5 mos.	186/138	
6 mos.	180/128	240/140
Clinical status after right nephro-omentopexy		
Subjective	Definitely improved. Rare headaches	No change
Objective	Decided improvement in eye-grounds	Advancing renal insufficiency. Eye-ground changes more pronounced
Interval between right nephro-omentopexy and left nephromyopexy	6 mos.	6 mos.
Status prior to left nephromyopexy		
Heart (EKG)	Normal	T changes more pronounced
Kidney function	Normal	Definite impairment. Urea clearance 30 per cent of average normal
Kidney biopsy (left)	Normal	Severe nephrosclerosis
Fundus	Minimal retinopathy	Severe retinopathy
Blood pressure after left nephromyopexy		
1 mo.	176/128	
2 mos.	192/136	
Clinical status after left nephromyopexy		
Subjective	Feels very well	Nausea and vomiting
Objective	Condition excellent	Rapidly progressive renal insufficiency
Remarks		Died 18 days after left nephromyopexy of retention uremia

Subjective Manifestations.—Six of the nine patients in this series were relieved of most of their symptoms for two to 11 months following the operation. The relief from headaches and vertigo was particularly striking in four patients (Cases 5 and 8, Table II; Case 6, Table III; and Case 9, Table IV).

TABLE IV

ESSENTIAL HYPERTENSION—RIGHT NEPHRECTOMY AND LEFT NEPHROMYOPEXY

Case	No. 9
Age and sex	53; M.
Duration of hypertension	1½ yrs.
Status prior to right nephrectomy	
Heart (EKG)	T changes
Kidney function	Urea clearance 40 per cent of average normal
Intravenous urogram	Right renal lithiasis
Kidney pathology (right)	Nephrolithiasis, chronic pyelonephritis, and chronic ureteritis
Fundus	Mild retinopathy
Blood pressure (av. 10 days preop.)	221/121
Blood pressure after right nephrectomy	
1 mo.	170/106
2 mos.	226/124
3 mos.	240/134
4 mos.	218/134
Clinical status after right nephrectomy	
Subjective	Headaches and vertigo have disappeared
Objective	No improvement in renal efficiency
Interval between right nephrectomy and left nephromyopexy	4 mos.
Status prior to left nephromyopexy	
Heart (EKG)	No further changes
Kidney function	Urea clearance practically the same as prior to right nephrectomy
Kidney biopsy (left)	Lost
Fundus	Mild retinopathy
Blood pressure after left nephromyopexy	
1 mo.	254/150
Clinical status after left nephromyopexy	
Subjective	Improvement persists
Objective	Condition excellent

Postoperative Anatomic Status of the Kidneys.—Intravenous urograms carried out from two to six months after nephro-omentopexy showed (a) little or no distortion of the renal calices; (b) apposition of omentum to the kidney as revealed by the position of the brain clips; this was verified in two necropsies; and (c) occasional ptosis of the kidney of a moderate degree; this was not accompanied by angulation of the ureter or by any clinical manifestations.

SUMMARY.—An attempt has been made to increase the vascularity of the kidney in nine patients with arterial hypertension by means of nephro-omentopexy and nephromyopexy. The clinical and experimental basis for these operations, the operative approach and the postoperative course, are described in detail.

Unilateral nephro-omentopexy is frequently followed by an appreciable fall in blood pressure which persists for two to three months following the operation but, in most instances, within six months the blood pressure usually returns to the preoperative level. It is too early to make any statement concerning the effect upon the blood pressure of the bilateral operations (three patients), only two months having elapsed since these were carried out.

Six of the nine patients in this series were relieved of most of their symptoms for two to 11 months following nephro-omentopexy. The relief from headaches and vertigo was particularly striking in four of these. Improvement in the degree of retinopathy was observed in two patients; pro-

gressive retinal lesions were noted in one. Cardiac and renal functions were not affected adversely nor was any improvement in their respective efficiencies observed.

Addendum.—Since this paper was submitted for publication, four of the nine patients alive at the time this paper was first written have been followed for an additional 15 months. None of these has died. The effect upon the blood pressure of the bilateral operations has been disappointing. The results were not unlike those already described for the unilateral operations. Within three to six months after the second operation (Cases 6 and 9), the blood pressure again returned to the preoperative level, although subjective improvement has continued in one of these (Case 6).

Two reports have appeared in the literature which deserve mention. Abrami and his co-workers[10] have reported their observations in two patients with hypertension treated by nephro-omentopexy. Their results are not unlike those reported in this paper. Mansfield, Weeks, Steiner and Victor[11] have recently shown that in seven dogs rendered hypertensive by Goldblatt's technic, pexis between the kidney and omentum or spleen was followed by a lowering in blood pressure. The reduction in blood pressure was more sustained in dogs with splenic pexis than in those with omental union.

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MALIGNANT MELANOMA*

A CLINICAL STUDY OF ONE HUNDRED SEVENTEEN CASES

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FROM the clinical and pathologic points of view melanomata are among the most important of any malignant tumors, affecting persons of all ages. They are one of the most malignant growths and the results obtained from treating them are generally known as far from satisfactory. Therefore, a special study of treatment of these lesions with more favorable outcome seems justifiable.

This is a study and analysis of a group of malignant melanotic tumors treated by surgery and showing the results of such treatment over various periods ranging from a few months to 13 years. While the number of cases analyzed is comparatively small, the end-results, where radical surgery has been employed, compare very favorably with results in treating other types of nonmelanotic malignant tumors.

The Term Melanoma.—According to scientific records, obviously, Hippocrates mentioned the appearance of melanoma first, but one may safely assume that others noted it before him because of its characteristic color and course.

F. Müller gave this type of tumor the name of "carcinoma melanodes," and the term melanoma was first used by Carswell, in 1836, and by Virchow.[1] In this paper melanoma is used as a term applying only to essentially malignant tumors.

Pigmented Naevus.—According to Kumer,[2] 32 per cent of melanomata derive from a naevus (naevo carcinoma); therefore, a brief review of the origin, pigment formation, and known causes of malignant degeneration of this type of lesion is desirable.

The pigmented naevus is characterized by the presençe of naevus cells in the corium which are more or less pigmented. Soldán,[3] 40 years ago, disclosed the nervous origin of the naevus clearly and convincingly. His work remained unnoticed until Masson,[4] 27 years later, identified his discovery and supported it with his own research. They demonstrated, without any doubt, that the naevi are the neuroma of the tactile end-apparatus (Wagner-Meissner and Merkel-Ranvier). The valuable research of Soldán[3] and Masson,[4] was confirmed by Foot.[6]

Laidlaw[7] drew a philogenetic parallel between the human and animal world, pointing out that, "the pigmented hairy mole appears to be a link or transition from pigmented tactile organs of the reptilian type to the hairy tactile organs

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of the mammalian type." Would this be the reversion to ancestral characteristics (atavism) like the development of supernumerary breasts[8] in the milk-line or at atypical locations; normally observed only in animals?

The formation of melanin pigment is probably a specific function of the basal cell layer of the rete malpighii. Melanin is supposed to be a pyrocatechol derivative closely allied to adrenalin. In animals, the mouth is often pigmented physiologically (for example, in dogs and cats). In human beings, pigmentation may be observed in the mouth in Addison's disease, lymphogranulomatosis, pediculosis, pernicious anemia, and malaria.

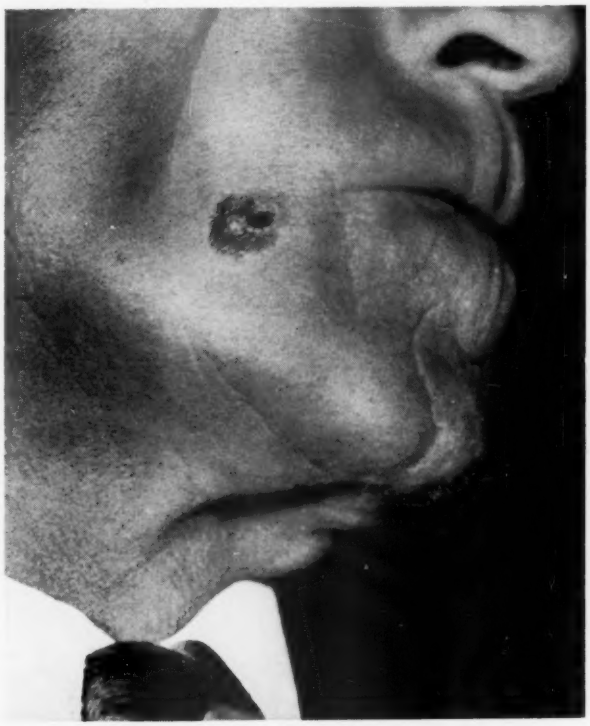

FIG. 1.—Photograph of a lesion in which repeated injury by shaving was most likely the inciting factor for the development of this malignant melanoma in a pigmented naevus. Wide local excision was performed. Patient is alive and well now for four years.

Etiology.—A melanoma often develops insidiously from a brown, black or bluish pigmented spot. Frequently, however, the wild proliferation of cells takes place after irritation or trauma, even from the unpigmented end-organs of the peripheral sensory nerves.[5] Repeated irritation over a period of years or following a single injury may be the cause, even in the very common mole with or without hair. The Cohnheim theory supposed that the pigmented mole harbors cells that are "sleepers" and after being irritated become actively growing melanoma. The cause may be friction by a corset on the back, or by the shoe in the nail bed (melanotic whitlow of Hutchinson), on the face after being cut by a razor (Fig. 1); even injection through a pigmented mole as in one of our cases seems to be the inciting cause.

Tièche[10] described a blue or bluish-black congenital macule located on the face, which is considered a persistent mongolian spot. The development of melanoma has occasionally been observed from this lesion. Infection of the surrounding skin areas of the naevus may be the irritating factor. The injudicious use of the electric needle (Fig. 2) in treating naevi was the most

FIG. 2.—Hosp. No. J. 795: Photograph of a nonpigmented melanoma with axillary metastases, developing from a pigmented papillary naevus due to repeated irritation by electric needle. The treatment consisted of weekly desiccation over a period of 11 months. Female, age 36, died with general metastases in five months.

probable originator of melanoma in five of our cases (4.3 per cent), and in 10 per cent of the cases reported by Adair.[11] One of our patients used a corn-plaster on a congenital pigmented mole, giving rise to the development of melanoma. Trauma seemed to be the etiologic factor in 28 (25 per cent) of our cases. Daland and Holmes[46] found it in 24.8 per cent.

According to F. C. Lee,[12] Anglo-Egyptian Negroes have 100 times as many melanomata as American Negroes.[13] The reason, he ascribes, is that the wearing of shoes by the latter prevents the direct irritation of rough roads and thorns. Parkes-Weber[14] reported a newborn baby who died of liver metastases of melanoma, whose mother died, after giving birth, of generalized melanosis. He supposed that the metastasis occurred during the intra-uterine life through the placenta. The pigmented areas of xeroderma pigmentosum may give rise to melanomata, as was also observed in one of our cases.

Pathologic Classification.—From the clinical point of view melanomata have been classified as follows[15]:

(1) Naevus giving evidence of increase in size or in darkening of pigmentation.

(2) Melanoma showing well-developed tumor in local lesion.

(3) Melanoma with involvement of regional lymph nodes.

(4) Generalized melanoma—melanosis.

All of our cases were of Groups 2, 3 and 4.

Age Distribution.—The youngest patient with melanoma in our series was a 15-month-old girl, then a five-year-old boy. The oldest was a man of 78 years. Among the remaining patients there seems to be a fairly even distribution of melanomata between the ages of 20 to 70 years in both sexes. The most frequent occurrence was observed between the ages of 45 and 60, in which group 38 per cent of our patients were found. Table I shows the distribution of our 117 patients according to age:

TABLE I

AGE DISTRIBUTION

Years of age	1–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80
No. of patients	2	8	19	20	23	29	13	3

The average age according to Hintze[16] is 47.7 years for males and 54.7 for females. Darier[17] states it to be 54.4 years for both sexes, while Butterwoth and Klauder[18] found it to be 49 years. Daland and Holmes[46] found their greatest number of cases in the sixth decade.

Statistics seem to indicate that women are affected somewhat more frequently.

Anatomic Distribution.—Melanomata may develop anywhere in the skin or, rarely, in mucous membrane. According to the analysis of our cases they are most common on the head (40 per cent), lower extremities (26 per cent), and upper extremities (15 per cent). According to the available computed figures, from the literature, melanomata are observed most frequently at the extremities (40.3 per cent: upper, 10.9 per cent; lower, 29.4 per cent). Properly speaking, the head lesions are the most frequent (35.1 per cent)—with the eye, 41 per cent, considered as one unit against four extremities. The remaining 24.3 per cent are scattered all over the rest of the body.

Melanomata have rarely been primarily observed at locations other than their usual appearance on the tegument. Peters reported five cases of melanoma observed in the male urethra. There have been fewer than 100 cases of melanoma of the rectum reported (Chisholm[21]). Lenče[22] collected 43 cases of primary melanoma of the central nervous system, in addition to one case of his own, also 11 cases in the biliary tract, and 39 cases in the oral cavity. They are seldom found in the nasal cavity, esophagus, or intestines. Tučzek[23] and Goldzieher[24] have described bilateral primary melanomata of the suprarenal glands.

Modes of Spread.—After the malignant changes have occurred in the tumor, they infiltrate the surrounding tissues, spreading first by *direct extension.* Handley[25] demonstrated the involvement of the lymphatic channels, which may result in the formation of numerous subcutaneous nodules proximally

or toward the periphery from the original growth. The tumor cells reach the *regional lymph nodes* through the skin lymphatics, causing their enlargement. It is rare to observe fungating lymph nodes because death occurs as the result of general metastases before this may happen. Pigmentation is often marked in the metastatic lymph nodes, even where the original lesion contained little or no pigment. The tumor gradually invades the capillaries of the invaded nodes, ruptures the blood vessels, and makes way for the invasion of the

FIG. 3.—Roentgenogram showing metastasis to the lower jaw from a malignant melanoma of the toe, which was cauterized, then excised by a chiropodist, later treated by an electric needle. Excision and resection of involved inguinal lymph nodes did not arrest the disease. Patient died three months later.

blood stream by the melanotic cells, which results in generalized metastases. Blood stream invasion may also occur directly.

Metastases—The Principal Organs Involved.—Among our cases, involvement of the regional lymph nodes at the time of the first examination was noted in 31 cases (27.4 per cent). Diffuse local, multiple involvement of the skin was present in two cases, and there were recurrent lesions in ten. Generalized metastases were observed in 11 cases, and these were considered inoperable (10 per cent).

Among Adair's[11] 400 cases there were 245 recurrent lesions, of which 141 were far advanced; he found only 26 per cent (that is, 105 cases) with primary tumors in operable condition.

According to Geschickter and Copeland,[26] bone metastases have been observed in only 1.07 per cent, which is about the same incidence as among our cases where we found only one metastasis of the lower jaw (see Fig. 3). This incidence, however, is possibly higher (Daland[46]).

Metastases usually appear in the regional lymph nodes of the drainage area. Lymph node metastases may occur early or it may appear only after the disease has become generalized. In generalized melanoma all organs may be involved. Diffuse and distant skin metastases are observed which vary in their course. Spontaneous regression[46] or sudden arrest of the evolution has been observed, which again may flare up with rapid growth. The liver is frequently invaded. The lungs, brain, heart, intestine, and the whole lymphatic system have been found involved.

Metastasis in the majority of cases appears within from six months to two years after the original tumor was noticed. It may, however, develop years after the original lesion has been removed or left untreated. In some cases the growth is slow and metastasis occurs late—in exceptional cases as late as from five to 15 years. Late, distant metastases are seen most often in the melanomata of the eye.[46] General metastases developed 27 years after operation in a case described by Balčerek.[27]

Symptomatology.—The first signs of the malignant proliferation are variable. It is common to observe that a hitherto symptomless naevus feels to the patient irritated, inflamed, and it may itch or even hurt slightly. It may ooze, weep or bleed, or adhere to the clothing. It increases in size, becomes more prominent, raised, and turgescent. A black spot may appear in the middle or at the periphery of the dark pigmented area (Fig. 1). The soft, cellular naevus becomes resistant, infiltrated, and firm. These changes are usually slow, taking several months; they are rapid only if irritation or trauma (especially if repeated) is the inciting factor.

Occasionally the original region is surrounded by small metastatic nodules which may be felt rather than seen. The lesion soon ulcerates, and becomes partly covered with a scab; it has the tendency to fungate and bleed easily. It is vegetant, gray-rose or dark red, and may be mistaken for a pyogenic granuloma. Regional lymph nodes are invariably enlarged after the disease advances. There can be no rule as to the time which has elapsed since the original lesion appeared. There seems to be no direct relation between the size of the tumor and the appearance of involved regional lymph nodes, which may occur earlier if ulceration has developed. General metastases may rarely occur simultaneously with regional lymph node involvement.

Melanuria, according to Kumer,[2] was present in 28 per cent of his cases. This may occur more often in the advanced lesions. The urine usually turns a darker color after standing in air, after the secreted melanogen becomes oxidized. Rarely, the urine is black from the secreted melanin.

There are some instances where the malignant degeneration of the pigmented mole is indicated by the enlargement of the regional lymph nodes,[15] and in some cases the original lesion may be so insignificant that it may not be detected even by careful investigation.

Time When Patients Apply for Treatment.—Less than 10 per cent of our patients came within one month following the first sign of malignant degeneration. The average time was eight months, which may be considered an unnecessary delay of six months, caused by lack of information or by fear.

Size of Melanomata.—Among our patients, at the time of applying for treatment, the size of the melanomata varied from 2 Mm. to 11 cm. in diameter. About 15 per cent of them had lesions measuring less than 1 cm. in diameter. The majority had lesions of from 1.5 to 2 cm. (55 per cent); the remaining 30 per cent had lesions averaging 3.5 cm. in diameter. No direct relation between the size of the lesion and regional lymph node involvement or general metastases could be established with any accuracy.

Clinical Types of Melanoma.—Usually, a melanoma is a flat or nodular, papillary, warty, raised lesion, but it may be a pedunculated, ulcerated, and less frequently a subcutaneous nodular lesion. It may be associated with neurofibromatosis or xeroderma pigmentosum. As has been mentioned, lymph node involvement may be the first symptom. Melanoma appears singly, and is seldom multiple.

Prognosis.—Melanoma is invariably fatal if not controlled by surgery or, possibly, by irradiation. It is not yet possible to depend entirely on the microscopic picture of the lesion regarding prognosis. General metastases occur more rapidly from an irritated lesion than from an untreated one. Some may live with untreated lesions for years, but the average duration of life is between one and one-half and three years. Younger people seem to die of the disease more quickly than do the more elderly.

A great number of patients who survive the five-year period develop recurrences later, and, according to Wilbur and Hartman,[28] all patients with melanoma of the eye die of general metastases (liver) if no other cause of death intervenes. One of our patients died six and one-half years after the operation, and one after 11 years from generalized melanoma.

Some recurrent lesions, however, may also be controlled and arrested by extensive radical surgery. Daland and Holmes[46] reported a patient with recurrent, diffuse, nonpigmented melanoma with inguinal lymph node involvement who, after the resection of the diffusely recurrent nodules of the thigh and leg, was well for six and one-half years.

Prophylactic Treatment.—Though the results obtained by surgery are encouraging, it seems to be equally important to prevent improper treatment or irritation of pigmented lesions. Collaboration between the public, practitioners, and surgeons is desirable with a view to eliminating those pigmented areas which may undergo malignant degeneration.

Beauty parlors, chiropodists, *etc.*, need to be warned about the possible consequences of insufficient treatment of the dark pigmented moles. It is

advisable to excise or coagulate those darkly pigmented naevi which are subjected to irritation (for example, by shoes, clothing, combing, and shaving). It is important to avoid the use of chemical irritations—caustics and electric methods which do not destroy the lesion in its entire extent.

FIG. 4 A

FIG. 4 B

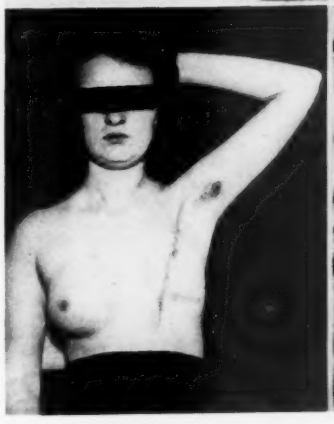

FIG. 4 C

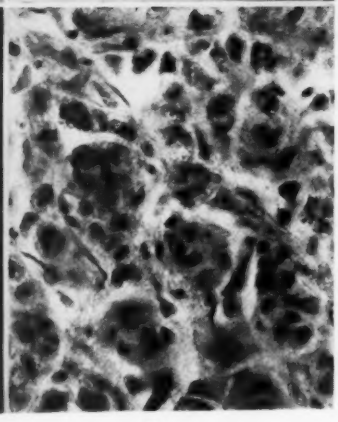

FIG. 5

FIG. 4 A.—Patient a 15-year-old girl: Malignant melanoma of three months' duration developing in a congenital naevus. Two months after local excision axillary lymph node dissection was performed. Several nodes were involved.

FIG. 4 B.—Local recurrence in ten months. Operative scar indicating previous excision and lymph node dissection in the axilla.

FIG. 4 C.—Good functional result after radical breast amputation for recurrence. Operative scar at the side of the chest indicates an electrosurgical excision for a third recurrence three months after radical operation. Prompt radical operation at the first intervention probably would have prevented repeated recurrences. Patient is well after one and a half years.

FIG. 5.—Path. No. S. C. 7966o: Photomicrograph of tumor showing cells in distinct groups. Hyperchromatism and anaplasia. Dark brown pigment in many cells. (×570)

Pigmented moles occur at an average number of 20 on the body of each individual (Block[9]); therefore, it is easy to see how frequently intervention may be abused.

Especially dangerous, clinically, are the black, glistening or deeply pig-

mented moles; however, there are observations of numerous darkly pigmented moles which have been quiescent for an entire lifetime.

Surgical Treatment.—The generally accepted treatment is surgical. Early, radical excision alone gives satisfactory results at present, but dissection of the regional lymph nodes, even if there are none palpable nor enlarged, is advocated. In a melanoma of the breast of a 15-year-old female (Fig. 4 A), in whom, in spite of the fact that there were no palpable or axillary lymph nodes, dissection was performed, but pathologic examination showed secondary involvement with heavy pigmentation (Fig. 5). Although, one year later (Fig. 4 B), and, again, 18 months later, local recurrences developed. Removal of the breast, and wide excision of recurrent nodules, was undertaken. The patient has been well for the past 18 months (Fig. 4 C). Local recurrence may be more effectively controlled when there has been a previous lymph node dissection.

Administration of Coley's serum is disappointing, as is the use of colloidal lead (Adair[11]). Amadon[29] and Adair[11] condemned electrocoagulation, but Pfhaler and the French school[30] rely entirely upon it. At the Radiumhemmet in Stockholm, electrosurgery is recommended, followed by irradiation.[41] Recent literature advocates electrosurgery as the most effective method to treat local lesions.

In our opinion, wide, radical excision of the primary lesion with the underlying fascia and surrounding subcutaneous tissues including its lymphatic area, followed by regional lymph node dissection, is the choice of treatment. If biopsy is necessary to establish the diagnosis, it should preferably be accomplished by an electric loop, followed by coagulation of the lesion, in order to prevent dissemination.

Amputation is advocated in melanomata of the fingers, toes and foot, if lesion is on the heel (Fig. 6), for anatomic reasons where the connective tissue bands going from the skin perpendicularly to the underlying bone form closed spaces filled with fat tissue. This arrangement directs any inflammatory process or new growth formation toward the periosteum. The same thing happens in cases of pyogenic infection of the fingers, especially on the volar surface. The infection, if not drained, generally involves the tendon sheath, periosteum and bone. Therefore, melanomata of the fingers, toes and heels, presumably, can be effectively eradicated only by amputation followed by regional lymph node dissection.

Among the reported cases, amputation was performed in six instances followed by inguinal lymph node dissection, in which involvement was found in three cases. Of the 25 cases reported by Williams[31] (including eight nonpigmented melanomata) the only one which survived had had amputation performed.

Regional lymph node dissection appears to be indicated especially in lesions of the extremities (particularly the foot) where constant irritation seems to predispose to earlier lymph node involvement. Melanomata of the face would seem to have, therefore, a better prognosis, as they are treated earlier and are

less subject to trauma, which may delay regional lymph node involvement. Daland and Holmes[46] reported three cases surviving the five-year period; after the involved regional metastatic lymph nodes were dissected. Table II shows an analysis of our 24 cases with lymph node dissection:

FIG. 6.—Photograph of a malignant melanoma of the right heel of two years' duration. Previous cauterization. Excision by the high frequency current, followed by inguinal lymph node dissection failed to arrest the disease. Six months later, recurrent nodules were excised from the leg, then from the thigh. This patient, male, age 56, died one year after the operation. Lived three years with the lesion. Amputation might have been a life-saving procedure.

TABLE II

ANALYSIS OF 24 CASES WHICH HAD REGIONAL LYMPH NODE DISSECTION

16 cases with involved lymph nodes..... 62.5 per cent
8 cases with hyperplasia..... 37.5 per cent

SURVIVAL AFTER LYMPH NODE DISSECTION WITH INVOLVED NODES

2 cases —No follow-up
6 cases*—Died after average period of 2 years
1 case —Died after 6½ years
7 cases —Alive (2, for 6 months; 1, for 2 years; 1, for 3 years; 1, for 5 years; 1, for 9 years; and 1, for 11 years)

* Advanced lesions.

SURVIVAL OF CASES WITH HYPERPLASIA

1 case —No follow-up
1 case —Recurrence 2 years later
4 cases—Died (1, after 10 months; 1, after 1 year and 10 months; 1, after 2½ years; and 1 after 6½ years)
2 cases—Alive (1, after 8 months; and 1, after 3 years)

To prevent local recurrences, more radical surgery, according to the principles of Handley[25] and Pringle,[32] seems to be justified. This consists of a wide dissection of the lymph channels, not only around the lesion but also up to the nearest lymphatic nodes. The skin is reflected on each side between

the lesion and corresponding regional lymph nodes, and the subcutaneous tissue removed with the subcutaneous fascia in one continuous strip. A specimen (melanoma of the upper arm, obtained from an operation in accordance with this principle), is shown in Figures 7 A and B. With such a method, Pringle operated upon two cases—one, a woman with axillary lymph node involvement, who has been well for 38 years; and the other, a man with inguinal lymph node involvement, who has been well for 30 years. He further stated that these two were the only cases he had ever operated upon. How much the

A B

FIG. 7 A.—Photograph of a malignant melanoma of the right upper arm, with axillary lymph node involvement, which developed in a naevus. First sign one year previously.

B.—Gross specimen removed by wide incision, with surrounding subcutaneous fat tissue ad fascia, block dissection of lymphatics from lesion to axilla, and axillary lymph node dissection. One lymph node showed involvement (with heavy pigmentation).

In this advanced lesion even such a radical operation failed to arrest the disease. Patient died one year later of pulmonary involvement.

more radical approach will improve the result can be answered only in the future, after more experience and follow-up observation.

Roentgen Ray and Radium Therapy.—According to Adair,[11] irradiation is of questionable value, and Stewart[34] states that only 2 per cent of melanomata have some degree of radiosensitivity. Darier even states that roentgen ray and radium treatment is harmful. Francis Carter Wood expresses his belief in its inefficacy. Meland[35] states that roentgenotherapy may destroy the local lesion but that all the patients die of general metastases. Holfelder[36] treated 18 patients, 14 per cent of whom had previously been operated upon, and 40 per cent died within the first year. Chaoul[37] (using daily doses of 300 to 500 r to a total of 8 to 15,000 r) treated 14 cases, and failed in only two instances. However, only one case survived four years, and the majority less than one year. McEuen[38] reported two cases out of six, well over five years after radiotherapy.

We may conclude that irradiation under the present technic is not recommended as the sole treatment of melanomata, although one may conceive that early, localized lesions may be destroyed with heavy radiation, which of course may be more conveniently excised radically with better ultimate and cosmetic results.

Analysis of Available Material.—There were 117 cases available for study from the records of the Skin and Cancer Unit of the New York Post-Graduate Hospital. In these cases the clinical diagnosis of melanoma was made. Of this series, only 81 have been verified by pathologic examination.

Six cases were admitted with general metastases for palliative treatment. In these cases only biopsies were taken.

Operations were performed upon 75 patients.

There was no operative mortality. Among these 75 cases, there were 15 patients woh did not return for follow-up examinations. The analysis of these cases is shown in Table III:

TABLE III

ANALYSIS OF 81 HOSPITALIZED PATIENTS

Total No. of patients admitted to hospital		81	
Inoperable, biopsy only		6	
No. patients operated upon		75	92.5%
Operative Cases:			
Postoperative deaths	0		
Died (with follow-up)	24		
Alive (with follow-up)	36		
No follow-up (lost)	15		
Total	75		
Cases with Follow-Up:			
Alive (after from 3 months to 13 years)	36		
Dead (after from 6 months to 11 years)	24		
Total	60		

GROUP A.—TIME-PERIOD OF POSTOPERATIVE FOLLOW-UP OF 36 PATIENTS FREE OF RECURRENCE OR METASTASIS

5— 3	months:	Toe, ear, cheek, foot, forehead
5— 6	months:	Breast, arm, temporal region, 2 on the foot
5— 1	year:	2 foot, back, 2 eye
7— 1½	years:	3 cheek, scalp, 2 arm, foot
1— 2½	years:	Toe
3— 3	years:	Forehead, foot, arm
1— 4½	years:	Arm
1— 5	years:	Forehead
2— 8	years:	Cheek, back
1— 9	years:	Forehead
2—10	years:	Arm
1—11	years:	Lip
1—12	years:	Arm
1—13	years:	Arm

Summary of the above: Head, 16 cases; extremities, 16 cases; elsewhere, four cases.

GROUP B.—TIME-INTERVALS BETWEEN OPERATION AND DEATH OF 24 PATIENTS WHO DIED OF THE DISEASE

1	died in	6	months
1	" "	9	months
1	" "	1	year
3	" "	1½	years
4	" "	2	years
6	" "	2½	years
3	" "	3	years
1	" "	4	years
1	" "	4½	years
1	" "	4¾	years
1	" "	6½	years
1	" "	11	years

GROUP C.—CASES FOLLOWED FIVE YEARS OR MORE, INCLUDING FIVE CASES WHICH WERE NOT TRACED AS ASSUMED DEATHS

Postoperative deaths	0
Known deaths	10
Assumed deaths (cases lost)	5
Well without recurrence	9
Lived with recurrence, until death 6½ and 11 years after operation	2
Total	26

5-year survival—42.3%
10-year survival—19.2%

These statistics are given with the lost (not followed-up) five cases which are considered as dead.

None of our cases lived free of disease over the five-year period having melanomata on the foot. In one case it was on the toe, which was amputated after a recurrent lesion, but the patient died 11 years later. Therefore, according to our small series of cases, we may reaffirm our previous statement that these malignant pigmented lesions are more benign in their clinical course on the head than when situated on areas such as the foot, where they are subjected to more trauma.

Among the patients in Group C, five had regional lymph node dissection; three of these five have survived for eight, nine and 11 years, respectively, with no evidence of disease, in spite of the fact that the regional lymph nodes were secondarily involved.

Five patients have been well for over ten years (one each for 13, 12, and 11 years, and two for ten years), one for nine years, two for eight years, and one for over five years. One died from general metastases 11 years after operation, following a symptomless period of eight years, and another died suddenly with general metastases after six and one-half years.

Statistics from Other Authors.—Darier[17] reported 43 cases, with follow-up on 23 of them. He employed electrosurgery, and had nine patients living for periods ranging from one to 12 years after operation. Miescher and Schürch[19] reported on 41 cases of melanomata on the head and extremities, treated by surgery and electrosurgery, and stated that 19 patients survived for periods varying from one to 11 years after operation (Table IV).

TABLE IV

SUMMARY OF CASES REPORTED BY OTHER AUTHORS WITH DEFINITE ARREST OF THE DISEASE FOR FIVE YEARS OR LONGER

Reported by	No. of Cases	Location of Lesion	Kind of Therapy	Survival		Percentage of 5-Year Arrest	Percentage over 10 Years
				No. of Cases	Time		
Adair[11]	70	Head, body and extremities	Surgery	23	5 yrs.	33	
Affleck[20]	170	Head, body and extremities	Surgery	20	5 yrs.	11.1	
Bloodgood[39]	200	Head, body and extremities	Surgery	1	5 yrs.	0.5	
Daland and Holmes[16]	82	Eye, head, body, and extremities	Surgery	15	5 yrs.	18.3	
de Cholnoky	26	Eye, head, body, and extremities, except eye	Surgery	11	5 yrs.	42.3	
				5	10 yrs.		19.2
Gleave[10]	18	Eye	Surgery	9	5 yrs.	50	
				5	15–19 yrs.		27
Hintze[18]	54	Head, body and and extremities	Surgery and x-ray	15	5 yrs.	27	
				5	13 yrs.		9.2
Meland[35]	50	Head, body and extremities	Surgery	9	5 yrs.	18	
Scharnagel[41]	70	Head, body and extremities	Electro-surgery and x-ray	27	5 yrs.	39	
Scott[42]	53*	Head, body and extremities	Electro-cautery	11	5 yrs.	37.9	
Total	793			156			
Average per cent of five-year arrest						19.2	

Differential Diagnosis.—Differentiation of melanoma from epithelioma is not difficult if pigmentation is present. The classic symptoms are well known. However, as Ewing has pointed out, there are pigmented epithelial tumors that are not identical with melanomata, and it is sometimes difficult to distinguish between them. These lesions are the pigmented epithelial papillomata, pigmented basal cell tumors, pigmented carcinoma in xeroderma pigmentosum.

Ulceration of the nail bed should be regarded with suspicion, especially above the age of 40, according to Womack.[43]

Ulcerated hemangiomata, warts, frequently granulation tissue, and above all pyogenic granuloma may closely simulate rapidly growing melanoma of the skin and mucous membrane. According to MacKee and Cipollaro,[44] the pyogenic granulomata, sometimes dry but mostly with mucopurulent exudate present, are soft (boggy), of various shades of red, often encrusted, and vary in diameter from 2 Mm. to 1 cm. They bleed readily and may be pedunculated. Melanomata grow relatively slowly; they are firmer, and discharge only if ulceration is present. Often, there is a history of an antecedent naevus with more or less pigmentation.

Histologic examination should confirm the diagnosis.

Nonpigmented Melanomata.—These are only rarely diagnosed clinically (3 per cent of our cases). The absence of pigment may be explained by their rapid growth—with bad prognosis. These melanomata are observed in patients past middle life. More than 50 per cent of them are at the lower extremi-

ties. Horwitz,[45] among his 49 cases, found that their life average was 18.8 months, and that the postoperative arrest in 10 per cent of his cases ranged from two weeks to six and one-half years. Of his cases, 80 per cent died in from seven to 25 months (average, 16.8 months) when only irradiation was resorted to (six cases). Of eight cases, in which surgical excision was followed

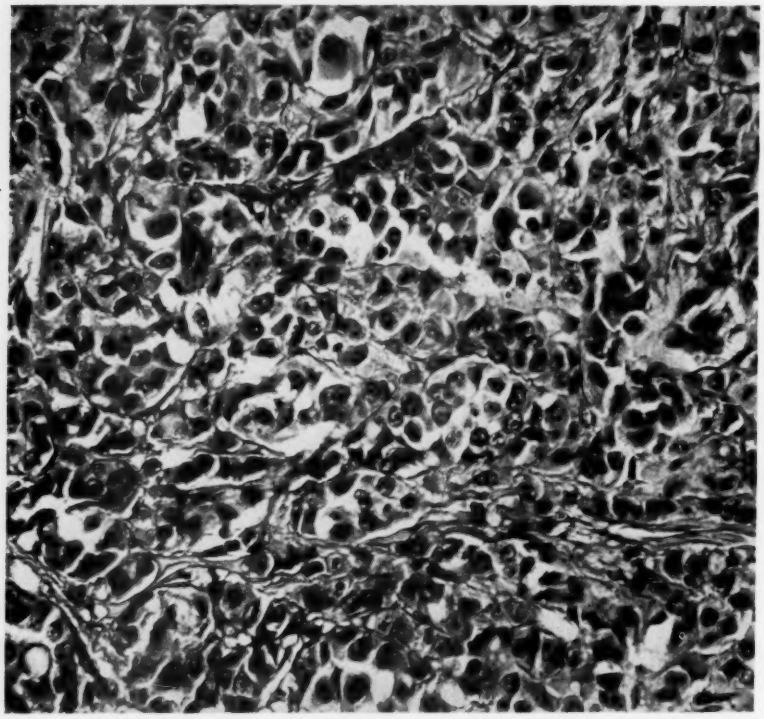

FIG. 8.—Path. No. S. C. 18683: Photomicrograph of a nonpigmented melanoma beneath skin of sole of foot. Female, age 68. Duration one year. (×250)

by roentgen ray and radium therapy, three were alive (for two years and 11 months, three years and eight months, and five years and nine months after operation).

Among our cases, there was a 55-year-old female with a nonpigmented melanoma. In this case, after amputation had been refused, 30 superficial, recurrent lesions were removed by an electric loop, at nine different intervals. The duration of the disease from beginning to end was three years. Only after two years was a lesion noted at the popliteal region, followed by others along the lymphatic path at the middle of the thigh within six weeks. The inguinal lymph nodes were involved for only a few months before the disease became generalized. Apparently, the tumor was spreading through the lymphatics of the subcutaneous tissues, and it could be clearly observed, clinically, that its propagation followed the lymphatics before the disease became generalized.

The study of this case and others suggest that amputation might have been a life-saving procedure.

SUMMARY AND CONCLUSIONS

Melanomata are pigmented or nonpigmented tumors of the skin and mucous membrane, supposedly of nervous origin. These extremely malignant lesions frequently arise from pigmented moles. They are observed at all ages, but predominantly between 45 and 60 years, and in both sexes.

Trauma and chronic irritation are evident in their development, as etiologic factors, in 25 per cent of cases. Lack of information is responsible for the fact that patients apply for late treatment. In the majority of cases there is an average of six months' delay. Since we are dealing with a superficial lesion that is easily discoverable, this dangerous delay could be prevented by disseminating information to the laity. Prophylactic treatment is advocated.

A clinical study and analysis of 117 cases of malignant melanoma are reported. Modes of spread, metastasis, symptomatology and prognosis are discussed.

Roentgen ray and radium therapy may destroy a local lesion, but authenticated cures under this treatment are rare; therefore, in operable cases it is not recommended in its present form.

In destroying the local lesion, electrocoagulation followed by lymph node dissection may be a desirable procedure.

In our opinion, radical surgery is the treatment of choice, and should consist of wide local excision including surrounding subcutaneous fat tissue and underlying fascia, followed by regional lymph node dissection. More radical intervention, consisting of removal of the lymphatic vessels in the subcutaneous fat tissues around the lesion and between the lesion and the regional lymph nodes, may also be desirable in irritated lesions. Amputation of the fingers, toes, and foot is advocated for anatomic reasons. This may give us improvement of the percentage of "five-year arrest," which to-day occurs in about one-third of the cases. The author's statistics of a relatively small number of cases show five-year arrest in 42.3 per cent, and ten-year arrest in 19.2 per cent of the cases; not including the cases untraced which are reported as deaths. In the New York Skin and Cancer Unit of the New York Post-Graduate Hospital, the tendency is to undertake radical surgery in treating melanomata.

The author wishes to acknowledge the kind cooperation of Dr. D. S. D. Jessup, Associate Consulting Pathologist of the New York Post-Graduate Hospital, who not only reviewed the slides of the cases studied but also gave many valuable suggestions in the preparation of this paper.

DISCUSSION.—Dr. D. S. D. Jessup (New York): There are some features of the pathology of melanotic tumors which are in contrast to the course pursued by other malignant tumors:

(1) The small and often insignificant size of the primary growth: One of our last treated cases had a tumor of short duration, 1 cm. in size, on the toe, which had already metastasized to the inguinal nodes. Another tumor, 3x5

Mm., under the nail bed of a finger, present for two months, showed invasion of the axillary nodes.

(2) The relatively benign appearance of the tumor cells in many melanomata: There are very few if any mitoses, anaplasia is absent, and in bleached sections, after removal of the pigment, the tumor appears relatively benign compared to what we are accustomed to see in metastasizing carcinoma or anaplastic sarcoma.

(3) In the metastases, we often find mere streaks of pigment in small cells as the only indication that the tumor is spreading from its primary site.

(4) Naevocarcinoma: While many believe that a large percentage of melanocarcinomata develop from pigmented naevi, it has been very seldom that we have been able to find traces of naevus cells alongside the developing melanocarcinoma. There is often the history of a pigmented birthmark but many of the deeply pigmented flat growths contain no naevus cells and show only pigmented cells in the corium. Where such pigment is deep in the corium we have the blue naevus, and if it is in the sacral region, the mongolian spot. Such pigmented areas may develop into melanocarcinoma, but we have followed many of the cases for years after removal of the tumor and they have shown no tendency to recurrence or spread. There does not seem to be any distinguishing feature in these flat melanomata which enables us to say whether they are potentially malignant. We see remains of flat melanomata alongside of more recent melanocarcinoma developing in the melanomatic bed, and we cannot differentiate the remains of the original growth from the clinically benign melanomata which have been treated by simple excision, and followed for years.

(5) Treatment: In following these treated cases for years, we have been impressed by the fact that surgery proves effective, often for long periods, and that regional node block dissections should be employed in the same way as in other forms of metastasizing carcinomata.

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SMOKING AND THROMBO-ANGIITIS OBLITERANS*

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TOBACCO SMOKING is so frequently associated with acute thrombo-angiitis obliterans that it is generally considered an important causative factor of the disease. The way smoking acts as a contributing or as an exciting cause is not known but it is essential for the success of treatment and the avoidance of recurrences that smoking be discontinued. Recent investigations[1] of the effect of tobacco upon the blood pressure, pulse rate and skin temperatures have demonstrated the same response in patients with thrombo-angiitis obliterans as in normal controls. Maddock and Coller[2] reported "comparatively analogous changes" from the pharmacologic action of intravenous nicotine. Hypersensitivity to tobacco[3] is not a factor in thrombo-angiitis obliterans and our results[4] with allergy tests did not confirm reports[5, 6] of increased sensitivity to tobacco.

Since almost all patients with thrombo-angiitis obliterans are cigarette smokers, it seemed to us that the changes in "The Blood in Thrombo-Angiitis Obliterans," which we recently reported,[7] might be the result of smoking. The blood changes were found in the acute, active stage of the disease. Not only was an excessive amount of tobacco being consumed, but inhalation of the smoke was unusually deep and frequent. The present study was made to determine the effect of smoking on the arterial and venous blood and the apparent physiologic responses.[8, 9, 10, 11, 12] No attempt was made to compare the various brands of cigarettes or the ingredients of the tobacco.

METHOD OF INVESTIGATION.—All patients were stabilized in bed at room temperature for one hour with the body and extremities covered by one sheet. Repeated observations were made on the blood pressure, pulse rate, respiratory rate and the skin temperature of the toes and fingers. Arterial blood was obtained from the right radial artery and venous blood from the right antecubital vein. The methods for collecting and analyzing the blood were the same as used in our previous work.[7]

After the period of stabilization and initial observations, the various procedures were followed with and without vascular puncture. Successive cigarettes were smoked at 15 minute intervals.

RESULTS.—*Peripheral Skin Temperature.* In a series of 14 normal control patients, the average decline in temperature of the toes was 2.8° C. and

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of the fingers 3.9° C. (Table I). With the smoking of successive cigarettes the temperatures frequently continued to drop until a level was reached which remained unchanged by further smoking, or which, as noted in Chart 1, returned to the initial level despite the continuation of smoking. In general, the most marked reduction in temperature occurred in normal, moderate smokers and not in the patients with neurocirculatory disease or in non-smokers.

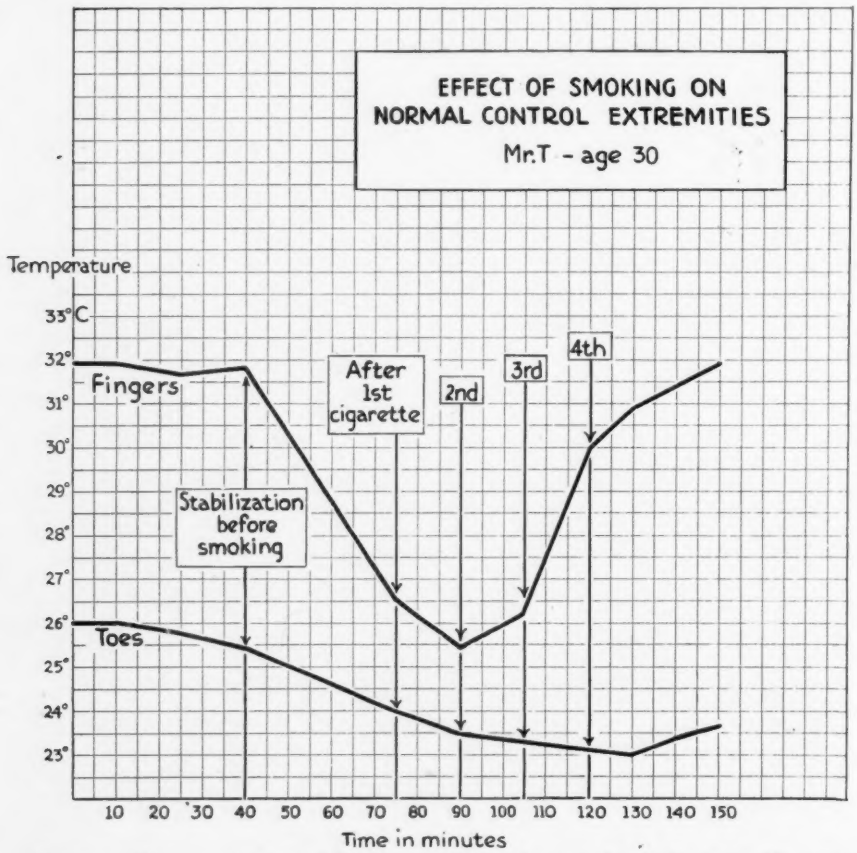

CHART 1.—Temperature curves of the fingers and toes of a normal control patient. The average temperature of the fingers dropped 6.4° C. after smoking one cigarette but returned to the presmoking level despite the continuation of smoking.

The response to smoking in patients with thrombo-angiitis obliterans varied with the stage of the disease and the amount of tobacco still being consumed. The skin temperature was reduced in 11 cases and elevated in eight cases. Although maximum declines in the temperature of the toes of 1.6° C. and of the fingers of 2.6° C. are shown in the table, these more normal changes occurred in clinically improved or recovered cases. These patients had some vasomotor response with novocain nerve block.[13]

The mechanism of reduction of the peripheral temperature is not entirely due to sympathetic control of the peripheral vessels. In Raynaud's disease,

TABLE I

CHANGES IN SKIN TEMPERATURES OF FINGERS AND TOES FOLLOWING SMOKING

	No. of Cases	Toes			Fingers		
		Max.	Min.	Average	Max.	Min.	Average
Normal controls							
Decreased temperatures	14	−4.0° C.	−0.1° C.	−2.8° C.	−6.4° C.	−0.1° C.	−3.9° C.
Increased temperatures	2	+0.2° C.	+0.1° C.	+0.2° C.	+0.3° C.	+0.1° C.	+0.2° C.
Peripheral circulatory disease							
Thrombo-Angiitis Obliterans:							
Decreased temperatures	11	−1.6° C.	−0.1° C.	−0.4° C.	−2.6° C.	−0.3° C.	−0.7° C.
Increased temperatures	8	+1.5° C.	+0.1° C.	+0.6° C.	+0.6° C.	+0.1° C.	+0.2° C.
Nonthrombo-Angiitis Obliterans:							
Decreased temperatures	8	−2.3° C.	−0.1° C.	−1.8° C.	−4.3° C.	−0.3° C.	−2.6° C.
Increased temperatures	2	+4.3° C.	+0.3° C.	+2.0° C.	+1.1° C.	+0.1° C.	+0.5° C.

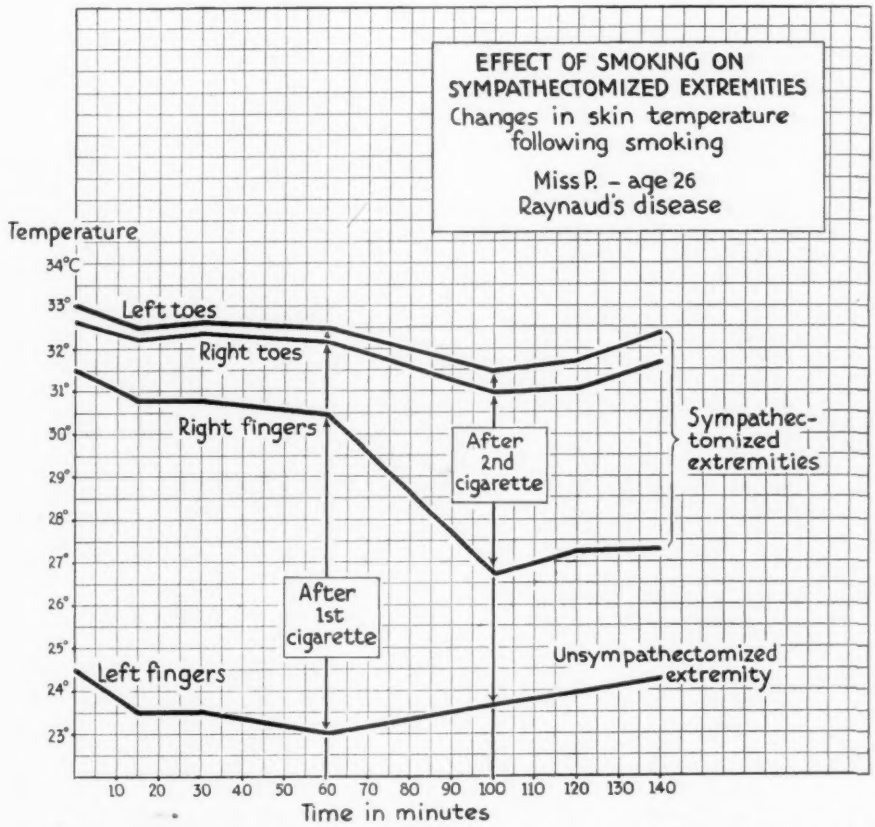

CHART 2.—Temperature curves of the fingers and toes on a patient with Raynaud's disease. The right upper and both lower extremities were sympathectomized and the left upper extremity was unsympathectomized. Note the marked reduction of 4.8° C. in the average temperature of the fingers of the sympathectomized right upper extremity after smoking one cigarette.

the sympathectomized extremities had an average decline in temperature of the fingers of 4.0° C. and of the toes of 1.5° C. (Chart 2) after smoking one cigarette. The left upper extremity was unsympathectomized. Smithwick, Freeman, and White[14] reported a similar response to adrenalin in sympathectomized extremities. The peripheral temperature response to smoking is due to changes in the circulating blood in addition to the central vasomotor control of the blood vessels.

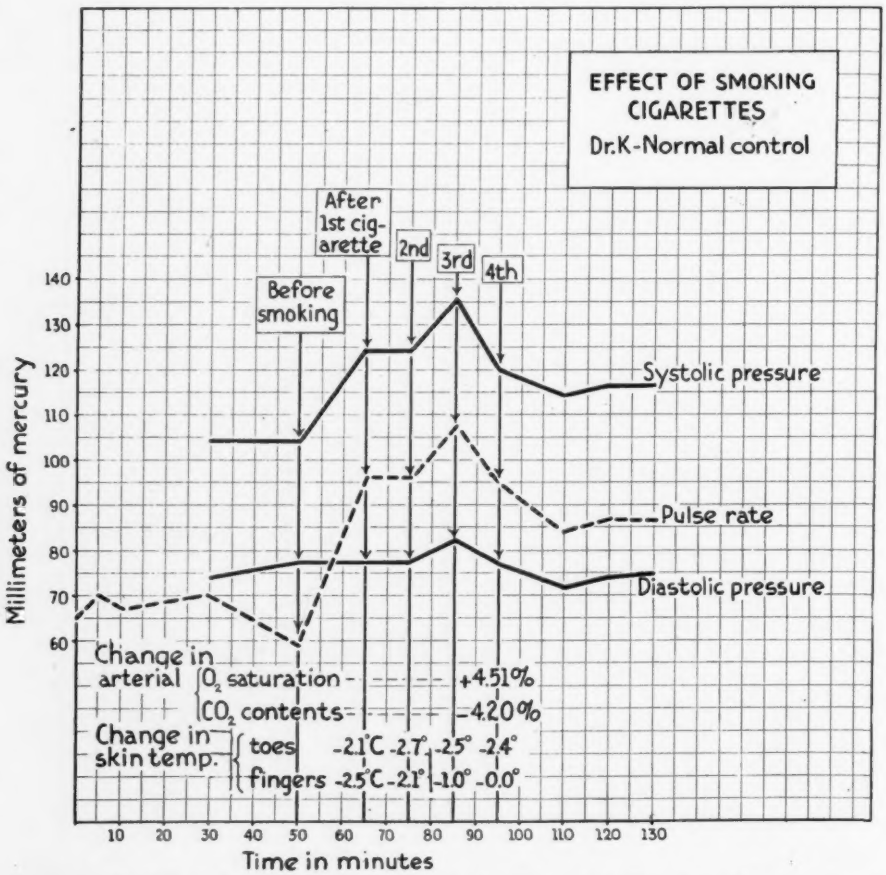

CHART 3.—Blood pressure and pulse rate curves showing the marked effect of smoking in a normal control patient which was accompanied by a 4½ per cent increase in oxygenation of the arterial blood.

Blood Pressure.—In the normal controls, smoking produced an elevation in pressure which was proportional to the initial readings and the number of cigarettes recently consumed. Low initial readings were usually obtained when smoking had been curtailed or discontinued. These patients showed the most marked but temporary elevation to the few cigarettes used in the test (Chart 3). High initial systolic pressure (160 to 180 Mm.Hg.) was occasionally found in heavy smokers and these patients had little, if any, response to the smoking test (Mr. P. Table V).

Patients with inactive thrombo-angiitis obliterans reacted in the same way as the normal controls (Charts 4 and 5). During the acute stage of the disease, all patients had systolic pressure of 115 to 135 Mm.Hg. After recovery when heavy smoking was resumed there was a gradual rise in pressure, and if smoking was not resumed the pressure dropped, in one case from 125 to 98. The blood pressure level seems to depend upon the adjustment of the body to the effects of smoking. It is significant that an acute attack of

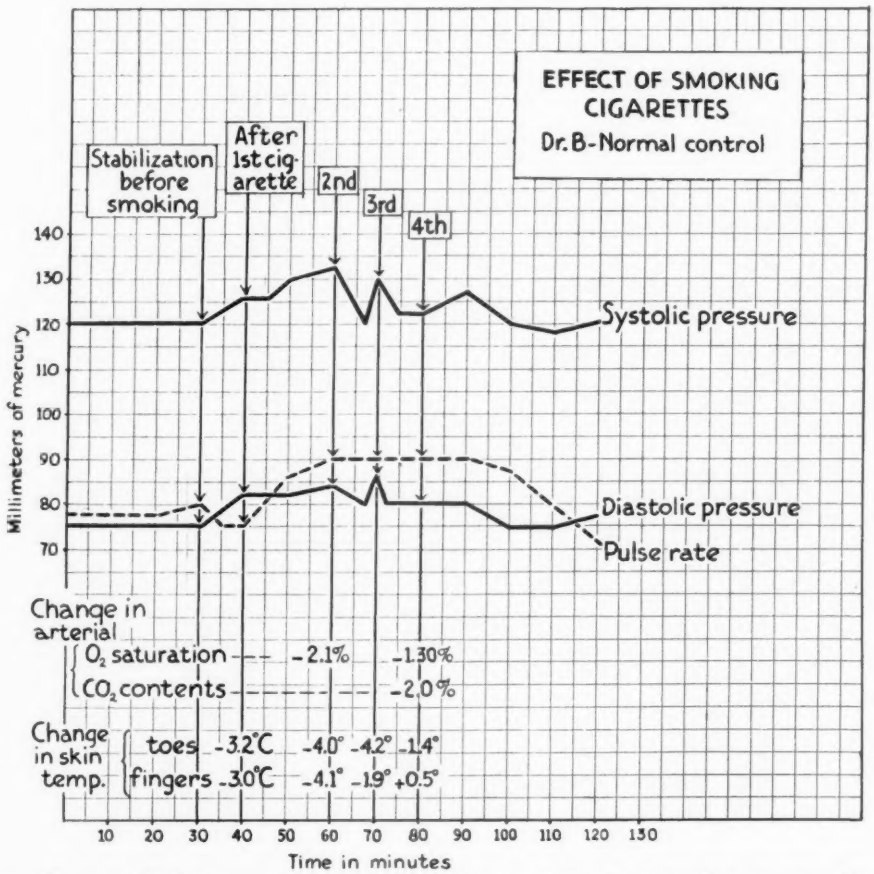

CHART 4.—Blood pressure and pulse rate curves of a normal control patient with 2 per cent reduction in the oxygenation of the arterial blood after smoking two cigarettes and only 1 per cent reduction after the fourth cigarette. The blood pressure had returned almost to its presmoking level after the third cigarette but the pulse rate remained elevated.

thrombo-angiitis obliterans, despite heavy smoking, was not accompanied by an elevated blood pressure.

Pulse Rate.—In patients with a normal or low initial pulse rate, smoking usually produced a tachycardia. The pulse rate, as a rule, increased with each cigarette until a level was reached which was not affected by further smoking. In thrombo-angiitis obliterans the pulse rate may be unaffected by smoking (Table V). As a rule the tachycardia disappeared with discontinuance of

smoking and as the normal rate was restored, smoking again produced an increase in the rate. The most marked response in pulse rate occurred among the moderate smokers whether normal controls or clinically recovered cases of thrombo-angiitis obliterans (Charts 3, 4, and 5).

Respiratory Rate.—The resting rate was not affected by smoking either in the normal controls or in patients with thrombo-angiitis obliterans. The average rate was 16 per minute.

Venous Blood.—In five of the six normal controls, and in all the improved

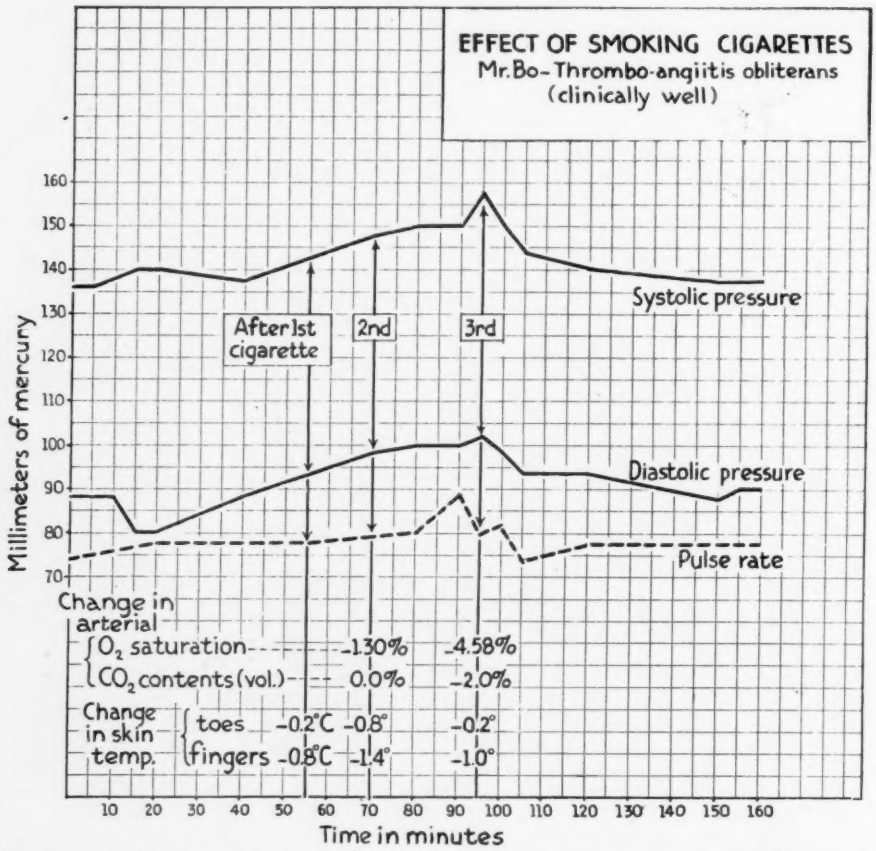

CHART 5.—Blood pressure and pulse rate curves of a patient with thrombo-angiitis obliterans. With the pulse rate unchanged after smoking there was a 1 per cent reduction in the oxygenation of the arterial blood after smoking two cigarettes and 4½ per cent reduction after the third cigarette.

and recovered cases of thrombo-angiitis obliterans the oxygen saturation of the venous blood[15] was higher after smoking (Table II). In one patient the venous blood contained 11 per cent more oxygen following the smoking of two cigarettes and 22 per cent more after four cigarettes. In two other cases there was a 22 per cent increase in oxygen saturation. We may assume that with excessive tobacco consumption the oxygen content of the venous blood may nearly reach the level present in the arterial blood.

TABLE II

CHANGES IN VENOUS BLOOD; OXYGEN AND CARBON DIOXIDE DETERMINATIONS, AND IN PERIPHERAL TEMPERATURES AFTER SMOKING

	Before Smoking O_2 Saturation	Number of Cigarettes Smoked	Change in O_2 Saturation Percentage	Change in CO_2 Content Vol. %	Average Change in Peripheral Temp. Toes	Average Change in Peripheral Temp. Fingers
Normal controls						
Mr. S.	61.20%	2	+ 8.70%	−2.79	−2.6° C.	.....
	87.40%	2	+ 4.10%	+1.58	−3.1° C.	.....
Mr. V.	56.00%	4	+ 4.93%	−2.33	−2.6° C.	−3.6° C.
Mr. M.	72.00%	4	+ 2.20%	+1.80	−2.2° C.	−1.4° C.
Mr. J.	30.86%	4	+14.60%	−0.36	0.0° C.	+0.3° C.
Mr. O.	83.16%	1	− 5.59%	0.00	+0.2° C.	+0.1° C.
Peripheral circulatory disease						
Thrombo-Angiitis Obliterans†:						
Active cases—smoking.						
Mr. P.	99.40%	4	−10.00%	+2.84	0.0° C.	0.0° C.
Mr. Nic.	77.23%	1	−12.52%	+3.33	−1.2° C.	−1.1° C.
		4	−20.97%	+1.16	−1.6° C.	−2.3° C.
Mr. Nie.	56.19%	2	− 3.91%	−2.11	.....	.....
Improved or recovered cases.						
Mr. B.	62.71%	2	+11.18%	−3.34	.....	.....
	31.00%	4	+22.60%	−7.12	+1.0° C.	−1.3° C.
Mr. M.*	61.36%	1	+ 0.79%	−3.15	+0.8° C.	−2.5° C.
Mr. S.	83.71%	4	+ 1.23%	−6.54	−0.8° C.	−1.7° C.
Mr. P.	64.65%	3	+ 6.85%	+0.16	0.0° C.	−0.6° C.
Nonthrombo-Angiitis Obliterans:						
Neurocirculatory.						
Miss K.	65.33%	4	+22.67%	−3.75	−0.9° C.	−0.9° C.
Senile arteriosclerotic.						
Mr. R.	59.37%	2	+ 1.13%	−0.15	−2.5° C.	−0.3° C.

* Became ill—nauseated, vomited and coughed.

† These patients were intensively treated with sodium tetrathionate which is prepared for us experimentally and supplied by G. D. Searle and Company of Chicago.

In three cases of acute thrombo-angiitis obliterans the opposite results were obtained. In one, there was 12 per cent reduction in oxygen saturation of the venous blood after smoking one cigarette and 21 per cent reduction after the fourth cigarette. The almost complete oxygen saturation, which we reported previously,[7] was present in the superficial venous blood obtained from the involved extremity and not from the right antecubital vein which was routinely used in this investigation. The average oxygen saturation before smoking was, however, higher than in the other series. These findings could be explained by slowing of the peripheral circulation or by interference with oxygenation of the arterial blood in the lungs, which reduces the oxygenation of the venous blood.[15]

Arterial Blood.—In four of five normal control patients the oxygen saturation of the arterial blood was less after smoking than before smoking. In the fifth case, increased saturation occurred but this change was accompanied by a marked elevation in blood pressure and increase in pulse rate (Chart 3). These latter changes may have been compensatory adjustments that caused the increased oxygenation.

TABLE III

CHANGE IN ARTERIAL BLOOD; OXYGEN AND CARBON DIOXIDE DETERMINATIONS, AND IN PERIPHERAL TEMPERATURES AFTER SMOKING

	Before Smoking O_2 Saturation	Number of Cigarettes Smoked	Change in O_2 Saturation Percentage	Change in CO_2 Content Vol. %	Average Change in Peripheral Temp. Toes	Average Change in Peripheral Temp. Fingers
Normal controls						
Dr. K. K.	91.89%	4	+ 4.51%	−4.30	−2.9° C.	−2.1° C.
Mr. O.	92.94%	1	− 0.86%	−1.19	+0.2° C.	+0.1° C.
Miss H.	91.37%	3	− 1.61%	−0.15	−2.6° C.	−4.3° C.
Dr. B.*	96.40%	1	− 2.10%	+0.21	.....	.....
		3	− 1.30%	+0.14	−3.9° C.	−4.1° C.
Peripheral circulatory disease						
Thrombo-Angiitis Obliterans†:						
Mr. Nie.	93.15%	2	− 5.15%	−0.16	.....	.....
Mr. B.	93.07%	3	− 2.14%	−3.50	−0.3° C.	−0.6° C.
Mr. P. (Smoking heavy)	95.19%	3	− 0.33%	−4.21	0.0° C.	−0.6° C.
Mr. Bo.	101.30%	2	− 4.40%	−1.41	.....	.....
	91.52%	2	− 1.30%	−0.02	−0.8° C.	−1.4° C.
		3	− 4.38%	−2.02	−0.2° C.	−1.0° C.
Mr. R.	91.45%	4	− 0.50%	−0.96	−2.9° C.	−0.9° C.
	91.91%	2	− 2.46%	+0.81	−1.3° C.	−1.3° C.
Mr. M.* (Not smoking)	80.95%	1	+11.17%	−0.45	+0.8° C.	−2.5° C.
Mr. B. (No smoking for 12 hrs., see Table V)	81.20%	2	+ 5.90%	−1.40	−0.7° C.	+0.2° C.
Nonthrombo-Angiitis Obliterans:						
Neurocirculatory.						
Mr. De M.* (Not smoking)	92.34%	2	+ 3.56%	−0.20	−0.9° C.	−1.0° C.
Senile arteriosclerotic.						
Mr. R.	91.64%	2	+ 0.32%	+0.21	−2.5° C.	−0.3° C.

* Became ill—nauseated, vomited and coughed.

† These patients were intensively treated with sodium tetrathionate which is prepared for us experimentally and supplied by G. D. Searle and Company of Chicago.

Patients with thrombo-angiitis obliterans showed the most marked reduction in the oxygen saturation of the arterial blood. As noted in Table III, the oxygenation of the blood was further reduced after successive cigarettes. No change occurred in a recovered case of thrombo-angiitis obliterans who had a blood pressure of 170/86 and who continued to smoke two or more packages of cigarettes daily. Two patients with thrombo-angiitis obliterans had increased oxygenation after smoking but the initial determinations were exceptionally low (80 and 81 per cent). Low oxygen saturation of the arterial blood was present in a number of clinically recovered cases of thrombo-angiitis obliterans when smoking had been curtailed or discontinued.

COMMENT.—Heretofore, the effects of smoking have been considered as individual systemic responses without correlating the usual complex protective compensatory adjustments which the body is capable of making to changing conditions. The physiologic reactions to smoking can be attributed to the deficient oxygenation of the arterial blood.[16] With smoking, the diminished oxygen supply is transitory in most individuals and rapid compensatory changes occur. The amount of tobacco consumed as well as the frequency of deep inhalation are probably important factors in the ability of the body to

TABLE IV

EFFECT OF SMOKING UPON NORMAL CONTROL PATIENTS

	Before Smoking	After Smoking			
	Stabilized Condition	1st Cig.	2nd Cig.	3rd Cig.	4th Cig.
Dr. K. K.—Moderate smoker.	Became slightly ill and dizzy during third cigarette.				
Arterial					
O_2 Saturation	91.89%	.....	.....	96.40%	.....
Change	.....	.....	.....	+ 4.51%	.....
CO_2 Content (vol.)	51.65%	.....	.....	47.35%	.....
Change	.....	.....	.....	− 4.20%	.....
Pulse rate	64	96	96	108	92
Blood pressure	104/76	124/76	124/76	136/82	120/78
Peripheral temp. (Av.)					
Toes	31.5° C.	29.2° C.	28.6° C.	28.8° C.	28.9° C.
Fingers	32.5° C.	30.2° C.	30.4° C.	31.5° C.	32.7° C.
Dr. B.—Moderately heavy smoker.	Became ill after fourth cigarette.				
Arterial					
O_2 Saturation	96.40%	.....	94.30%	.....	95.10%
Change	.....	.....	− 2.10%	.....	− 1.30%
CO_2 Content (vol.)	42.57%	.....	42.78%	.....	40.58%
Change	.....	.....	+ 0.21%	.....	− 1.99%
Pulse rate	82	76	90	90	90
Blood pressure	120/76	126/82	132/84	130/86	122/80
Peripheral temp. (Av.)					
Toes	33.0° C.	29.8° C.	29.0° C.	28.8° C.	31.6° C.
Fingers	33.6° C.	30.5° C.	30.4° C.	31.6° C.	34.0° C.

make the adjustments. These factors naturally differ in each individual and with each type of smoking. Continual failure of systematic responses to compensate for the decreased oxygen tension in the tissues and internal organs may produce metabolic disturbances throughout the body.[17]

In acute cases of thrombo-angiitis obliterans as previously reported by us, acapnia may be present. As noted in Table III, the oxygen saturation of the arterial blood was reduced as much as 5.15 per cent after smoking only four cigarettes. Compensatory adjustments in blood pressure, pulse rate, respiratory rate, red blood counts, acclimates the individual to the reduced oxygen supply. Any one or more of these systemic adjustments may be inadequate but this is compensated for by greater changes in the others. Tachycardia, hypertension, polycythemia, or increased respirations may all contribute in supplying sufficient oxygen to the tissues.

In thrombo-angiitis obliterans a polycythemia was occasionally present in the improved or recovered stage of the disease. During the acute stage there was usually an anemia which was not amenable to recognized hematopoietic stimulants. Although the changes in erythrocyte counts which followed the smoking tests were inconstant, the pulse rate and the blood pressure were definitely affected by smoking. The efficiency of the compensatory mechanisms for anoxemia seems to be the determining factor in the development of the disease.

Females, whether smokers or nonsmokers, responded more actively to smoking than did males. In all cases thus far examined, there was an active

TABLE V

EFFECT OF SMOKING UPON PATIENTS WITH THROMBO-ANGIITIS OBLITERANS

	Before Smoking	After Smoking			
	Stabilized Condition	1st Cig.	2nd Cig.	3rd Cig.	4th Cig.
Mr. R.—Clinically improved.					
Arterial					
O_2 Saturation	91.91%	.....	89.45%	87.81%	.....
Change	.....	.....	− 2.46%	− 4.10%	.....
CO_2 Content (vol.)	50.10%	.....	50.91%	50.72%	.....
Change	.....	.....	+ 0.81%	+ 0.62%	.....
Pulse rate	80	80	80	80	.....
Blood pressure	110/60	110/60	120/60	124/60	.....
Peripheral temp. (Av.)					
Toes	29.6° C.	29.9° C.	28.8° C.	28.8° C.	.....
Fingers	33.5° C.	33.2° C.	32.3° C.	33.0° C.	.....
Sedimentation time	1 hour 45 minutes				
Mr. Bo.—All four extremities involved. Clinically well.					
Arterial					
O_2 Saturation	91.52%	.....	90.22%	86.94%	.....
Change	.....	.....	− 1.30%	− 4.58%	.....
CO_2 Content (vol.)	42.43%	.....	42.41%	40.41%	.....
Change	.....	.....	− 0.02%	− 2.02%	.....
Pulse rate	77	78	80	80	80
Blood pressure	138/88	142/92	148/98	158/102	136/94
Peripheral temp. (Av.)					
Toes	29.8° C.	29.9° C.	29.3° C.	29.9° C.	30.8° C.
Fingers	31.9° C.	31.2° C.	30.6° C.	31.0° C.	31.9° C.
Sedimentation time	1 hour 45 minutes				
Mr. Br.—Acute case. Smoking markedly curtailed—almost complete abstinence from previous two or three packages per day.					
Arterial					
O_2 Saturation	81.20%	.....	87.10%	.....	86.20%
Change	.....	.....	+ 5.90%	.....	+ 5.00%
CO_2 Content (vol.)	47.10%	.....	45.70%	.....	46.40%
Change	.....	.....	− 1.40%	.....	− 0.70%
Pulse rate	84	87	90	88	86
Blood pressure	128/86	134/86	144/90	.....	138/86
Peripheral temp. (Av.)					
Toes	32.5° C.	32.2° C.	31.8° C.	31.6° C.	29.5° C.
Fingers	33.4° C.	33.6° C.	33.6° C.	31.0° C.	33.3° C.
Sedimentation time	25 minutes	.....	.....	.....	25 minutes
Red blood counts (millions)	3.9	.....	3.7	.....	3.9
Change	.....	.....	− 0.2	.....	.....
Reaction of the blood (pH)	7.48	.....	7.52	.....	7.52
Mr. P.—Heavy smoker. Right leg previously amputated. Clinically well.					
Arterial					
O_2 Saturation	95.19%	.....	.....	94.86%	.....
Change	.....	.....	.....	−0.33%	.....
CO_2 Content (vol.)	46.68%	.....	.....	42.47%	.....
Change	.....	.....	.....	− 4.21%	.....
Venous					
O_2 Saturation	64.65%	.....	.....	71.50%	.....
Change	.....	.....	.....	+ 6.85%	.....
CO_2 Content (vol.)	49.11%	.....	.....	49.27%	.....
Change	.....	.....	.....	+ 0.16%	.....
Pulse rate	70	70	70	76	.....
Blood pressure	170/86	178/86	170/86	170/86	.....
Peripheral temp. (Av.)					
Toes	30.7° C.	31.1° C.	31.2° C.	31.5° C.	.....
Fingers	33.3° C.	33.0° C.	32.6° C.	32.8° C.	.....
Sedimentation time	2 hours 15 minutes				

response in the pulse rate, blood pressure and peripheral temperatures, contrasting in this respect to the occasional exceptions in men. This may bear a relation to the fact that thrombo-angiitis obliterans rarely occurs in females.

The deleterious effect of smoking may be due to reduction in oxygenation of the arterial blood. Physiologic responses may overcome the interference with the oxygen absorption in the lungs or the entire body may become adjusted to the reduced oxygen tension in the tissues. Transitory lowered oxygen tension in moderate smokers probably has no ill effects, but Cannon[18] and his coworkers[19] believe that deficient oxygen supply to the liver, adrenals and intestines definitely contribute to rapid coagulation of the blood. There is evidence that adrenal dysfunction may be an etiologic factor in thrombo-angiitis obliterans. The usual changes in blood pressure, pulse rate, peripheral circulation, and the blood sugar[20, 21, 22] which follow cigarette smoking could be due to increased epinephrine output. Further, sympathectomized extremities responded to smoking in a similar fashion to the response to adrenalin.[14] In the acute stage of thrombo-angiitis obliterans adrenal dysfunction may be responsible for the absence of these responses. The characteristic dark blood in the acute stage is also found to be present in adrenalectomized animals.[23]

SUMMARY AND CONCLUSIONS

Tobacco smoking was usually accompanied by a greater reduction in the oxygenation of the arterial blood in patients with thrombo-angiitis obliterans than in normal individuals. The extent of the reduction seemed to be influenced by physiologic adjustments in the blood pressure, pulse rate, and peripheral skin temperatures.

Occasionally, when a marked increase in blood pressure and pulse rate followed smoking, the oxygen saturation of the arterial blood was found to be increased. The increased oxygenation was greatest in recovered cases of thrombo-angiitis obliterans who, after a period of abstinence from smoking, had particularly low oxygen saturation.

Decreased utilization of oxygen by the superficial tissues is indicated by the increased oxygen saturation of the venous blood associated with a decline in peripheral temperatures.

Failure of physiologic adjustments to compensate for the lowered oxygen tension in the tissues and internal organs may be an etiologic factor in thrombo-angiitis obliterans. The increased viscosity and other changes in the blood in thrombo-angiitis obliterans which we recently reported may be evidence of disturbed tissue metabolism.

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THE RATE OF HEALING OF TENDONS*

AN EXPERIMENTAL STUDY OF TENSILE STRENGTH

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THE PROBLEM of tendon healing and the various factors which affect it are still quite unsettled. Despite a great number of experimental and histologic studies which have appeared during the past 30 or more years, there is still lack of agreement concerning even the tissues which take part in the process. It is not necessary here to review the entire problem, which has been gone into in detail elsewhere (Mason and Shearon). The articles by Schwarz, F. Hesse, Biesin, Salomon, Närvi, Garlock, DeBarnardis, and others present extensive and exhaustive reviews to which the reader is referred. It may not be out of place, however, to outline very briefly the present status of the problem of tendon repair sufficiently to provide a background for the problem which we are now reporting.

Three tissues may take part in tendon repair—the tendon itself, the connective tissue in and on the surface of the tendon, and the connective tissue surrounding it. Various other cellular elements enter into the process, but the three mentioned are the important ones. Great difference of opinion exists, however, as to the part played by these various tissues in repair. The earlier workers thought that the tendon cells were the most important element in repair and that the connective tissues played a minor rôle. Recent workers, however, generally agree that the connective tissue elements are of great significance and many even deny that the tendon itself takes any part. In fact, many believe that tendon healing is simply scar tissue formation, similar to that occurring elsewhere, except for the fact that the physiologic requirements of this scar cause it to become equivalent to tendon. Others feel that while the connective tissues take part, they do not form ordinary scar but a specific tissue, in a manner similar to the periosteum. A few, like ourselves, have concluded that both the connective tissues in and about the tendon and the tendon itself take part in the process and that both are important.

From the standpoint of tissue participation, tendon healing may be divided into two stages. The first stage is the connective tissue stage, in which the connective tissues in, on, and about the tendon proliferate to form a fibroblastic cuff and scar about and between the tendon ends. This stage of repair comprises the exudative phase and the phase of fibroplasia and

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terminates on the fourteenth to sixteenth day. The second stage of repair is dominated by processes going on in the so-called tendon callus which result in the conversion of this tissue into tendon. This is the formative stage or the stage of organizing differentiation. It is in this stage of regeneration or healing that we should look for evidences of specificity of tissue. It is our feeling that specific regenerative processes in the tendon dominate this stage. While histologic evidence of tendon cell proliferation may be found as early as the fourth or fifth day, their organization of the union becomes dominant on about the fourteenth day. If our concept of the process is correct, the new tissue uniting the stumps is true tendon, in the same way that bone callus becomes true bone. If this tissue is simply scar, some explanation must be given for its developing, histologically, into tissue almost indistinguishable from normal tendon.

Whatever the tissue is which eventually forms to unite the stumps, whether it be simply a scar or true tendon, there seems to be general agreement that it behaves as tendon and possesses the strength of tendon.

Out of a great amount of experimental data and philosophic discussion, there emerges, particularly, the question as to the significance of function on the process of tendon repair. The importance of function was emphasized by W. Roux, who stressed its value in maintaining tissue and in stimulating growth in normal tissue. Roux's ideas were introduced into clinical surgery by Wolff, who established the trophic principle of function as the factor which determines the character of supporting structures. Although he had in mind particularly the effect of function on the final form and structure of callus and bone, there is no doubt but that his conception of functional influence encompassed the whole of scientific medicine and general biology.

Many experimental studies have been carried out in an effort to determine the rôle function plays in the formation of tendon. E. Rehn demonstrated that under the influence of function connective tissue strips were converted into tendon-like structures. Similar results were obtained by Schwarz and Hueck. Hesse demonstrated that tendons transplanted into the knee joints of rabbits and dogs maintained their tendinous structure and if divided healed like tendon provided they were subjected to tension; whereas, if they were not subjected to tension, they soon regressed into ordinary fibrous tissue. Bier and Salomon insisted that tendon regeneration was specific and could proceed without function. They conceded, however, that while function was harmful during the first phase of healing, during the second phase or stage of differentiation it exerted a generally increasing influence in the sense of further differentiation, maintenance, and increase in the already laid down tissues. O. Levy concluded that function came into play only when organs begin to function. Hauck reached somewhat similar conclusions. Biesin concluded that fibrous tissue or the scar uniting tendon ends became tendon or at least differentiated into tissue equivalent to tendon under the influence of tension and use. Kleinschmidt showed that fascia lata

of the rabbit when grafted into a defect of the quadriceps muscle maintained those fascial layers which paralleled the line of pull of the muscle. Eventually, the whole fascial graft was replaced by connective tissue, but the effect of function on it was clearly demonstrated.

Studies on the effect of function on tendon healing and regeneration have dealt largely with observations on the gross and microscopic anatomy of the replacement tissues. It is common observation that after healing the newly formed tissue looks like tendon but never actually reaches a stage where it cannot be distinguished from it. Histologically, it is claimed that it can be distinguished from normal tendon even as long as one year after repair. No one, however, so far as we have been able to find, has made any detailed observations on the tensile strength of the new tendon or of the tendon union to determine just how closely it approaches that of normal tendon. Garlock, in 1927, as the result of an extensive series of experiments, concluded that after the fourth day "the scar tissue of itself becomes the bulwark in the maintenance of the continuity of the tendon. With stress and strain applied on the fifth day, in the form of passive motion (in experimental animals only) it appears from the sections that the scar joining the tendon ends stretched somewhat but not to any marked degree. . . . Following the fifth day the scar tissue between the divided ends of the tendon progressively increases in strength and density up to the day when the union is as firm as it will ever be." Mason and Shearon, in 1932, made a few observations on the gross amount of pull required to fracture the healing tendon or graft. They found that in the early stages the surrounding tissues were important but that later the tissues in the gap gained great strength. From the fourth to eighth day rupture occurred with pulls of 2½ to 4½ pounds, while after the second week pulls of 16 to 40 pounds were required. No attempts were made, however, to correlate these pulls with cross-sectional areas of the tendons nor, except in a general way, with the phases of repair.

The method for studying the rate of wound healing by determining tensile strength during various phases of healing was introduced by Harvey and by Howes, Sooy and Harvey, in 1929. They showed that the tensile strength of healing wounds in the skin, fascia, muscle, and stomach followed a curve similar to that determined by Carrel, Spain and Loeb, Carrel and Hartmann, duNoüy, Clark, Lumière, and others. They found that there was first a quiescent period or lag during which tensile strength was due entirely to the sutures. This lag period lasted four to six days and was followed by a proliferative phase characterized by a rapid increase in tensile strength, which produced a curve of progressively decreasing velocity to reach a maximum at about the fourteenth day, at which time many tissues will have regained normal strength. They also noted, however, that a third phase, "the phase of maturation," occurred, during which time structures such as bone and tendon regained their normal strength. This method of determining the rate of healing has now come into general use.

Personal observations made during earlier experiments with tendons indicated that the tensile strength was constantly increasing beyond that shown at the end of two or three weeks, and it was suspected that there would be two phases in the curve of increase in tensile strength. Experimental work reported by Howes, Harvey and Hewitt, in May of 1939, has shown that in cutaneous wounds of dogs, cats, rabbits, guinea-pigs, and rats the curve of healing as determined by tensile strength showed two rises. The first rise due to fibroplasia began about the fifth day and reached a maximum on the twelfth to fourteenth day. The second rise began on the eighteenth to twenty-second day, except for the guinea-pig in which it began on the thirtieth day. This rise indicated the stage of organizing differentiation, by which the tissue regained its normal strength. It was associated with histologic changes whereby the "entire architecture is differentiated without a vestige of embryonal pattern." The collagenous fibers become larger, blood vessels fewer and a tissue closely resembling but not quite identical with the normal results. This second phase of organizing differentiation lasts until normal strength is regained—in the rat in 60 days, in the rabbit in 180, while in the dog the scar does not regain the normal strength of the skin even after 358 days.

The second phase of increase in tensile strength would seem to correspond in its onset with the time when the tenoblastic phase in tendon healing becomes the most important. We should expect to find, therefore, a curve in tendon repair similar to that found by Howes, Harvey and Hewitt in the skin. It is this phase of repair, that of organizing differentiation or maturation, which histologic studies show to be especially influenced by function; and if function does accelerate differentiation, we should be able to detect it by a study of the tensile strength of healing tendons.*

* The tensile strength of any particular tendon is difficult if not impossible to determine; and after a study of the reports in the literature and personal experimentation, we are inclined to agree with Cronkite that a norm cannot be established. Gratz has made a number of important contributions on the subject of the strength of fibrous tissues and has made an exhaustive study of tendon strength in man and various domestic animals. He found that certain fibrous tissues "withstood stress up to a maximum of 1,476 Kg. per sq. cm. (20,959 pounds per sq. in)." Many tissues exceeded this figure. Nicola reported on the strength of four human tendons with an average tensile strength of 7,330 pounds per sq. in. (645 Kg. per sq. cm.). Cronkite measured the tensile strength of 294 human tendons, some fresh, but for the most part dissecting room material. He found considerable variability not only in different cadavers, but in specimens from the same cadaver. Thus, the range for the whole series was from 4,000 to 30,000 pounds per sq. in. while the averages ranged from 8,700 to 18,000 pounds per sq. in. (611 to 1,265 Kg. per sq. cm.). We made attempts to obtain the tensile strength in a number of normal dog tendons utilizing, as a rule, several segments from each tendon. Our results indicated a tensile strength which varied from 3,250 to 18,170 Gm. per sq. Mm. and averaged 9,386 Gm. per sq. Mm. in 15 fresh tendons. We have also tested human tendons taken from a dissecting room cadaver. Cronkite has shown that the tensile strength in these tendons is approximately the same as in fresh tissue. Our figures ranged from 6,540 Gm. per sq. Mm. (9,281 pounds per sq. in.) to 25,490 Gm. per sq. Mm. (36,140 pounds per sq. in.).

In this series of experiments an attempt has been made to ascertain the rate at which the healing sutured tendon regains its tensile strength. The work has been carried out upon the dog, using, in 16 experiments, the extensor carpi radialis tendon, and, in 94 experiments, the flexor carpi ulnaris. In each case the tendon was exposed under aseptic precautions with the dog under intravenous nembutal anesthesia. The tendon sheath was split open for a distance of about 5 cm., the tendon separated from its mesotenon and divided transversely with a sharp knife. The ends were immediately united

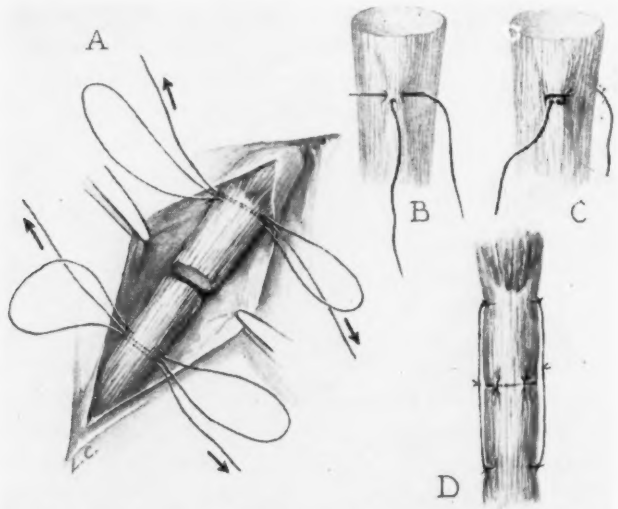

FIG. 1.—Showing the method of tendon repair, whereby the tension sutures pull transversely to the tendon fibers. A small bundle of fibers is caught at the side of the tendon about 1 cm. from the divided end. The suture is then passed straight through the tendon to emerge on the opposite side. A second suture is then taken and a small bundle of fibers is caught just below the point of emergence of the first suture, between it and the end of the tendon. The second suture is then passed straight through the tendon and emerges above the knot of the opposite suture and between the fiber bundles which have been caught in it. When each suture is drawn toward the cut end of the tendon, it rides over the knot of the opposite suture, as if over a pulley, and the longitudinal pull is converted into a transverse one. Accurate approximation of the tendon ends is obtained by a few fine silk sutures which unite the peritendinous tissues at the site of apposition.

with No. 8, Champion, twisted, untreated silk. The type of suture in all but six instances was that recently described by one of us. It consists of a pair of transverse sutures introduced into the tendon about 1 cm. above the cut end in such a way that one emerges from the side of the tendon above the knot of the opposite suture and is held there by the tendon fibers which have been grasped in the knot (Fig. 1). In this manner, the line of pull of the suture is transferred from a longitudinal to a transverse direction. This suture will rupture at the knots with 5.23 pounds without pulling out of the tendon. Despite the fact that the suture breaks, we believe that finer sutures are indicated. This method of suture possesses the advantage of leaving free the tendon ends which we wish to take part in the healing process. There

is no disadvantage to the length of suture lying on the outside of the tendon. The sutures are soon covered by a thin sheet of tissue and when healing is complete lie embedded apparently under no tension on the surface of the tendon without causing any interference with gliding action.

Following suture the sheath is not closed, but the subcutaneous fatty tissues are approximated over the suture site, and the skin is closed with silk. A pressure dressing is applied, and a plaster bandage applied to the leg to hold the sutured tendon in relaxation.

The wounds were reopened under aseptic precautions at intervals varying from two to 68 days, and the sutured tendon was examined and removed. The gross amount of reaction was noted, the amount of separation between the stumps measured, the width of the stumps was taken, and measurements made of the distance of the sutures from the tendon ends. The stumps were then fastened as securely as possible in hemostats and attached to a spring scale where tension was slowly applied until separation started, which point was taken as the measurement of tensile strength. In some specimens it was not possible to rupture the complete tendon by our apparatus. In many of these instances the tendon was divided longitudinally and a small segment was subjected to the experimental pull.

The sutures were not divided before testing the strength although in a few instances one or both had broken or untied before the tendon was removed. The measurements and observations given, therefore, record the strength of the tendon plus that added by the suture. It was believed that in this way a truer idea of the clinical situation could be gained. We were also able to make some observations on the holding power of the tendon for the suture, a factor we believe to be of clinical importance.

In a number of the earlier experiments we simply recorded the number of pounds or ounces needed to break the tendon. This holds true especially for the two- and seven-day specimens in which we have only the measurements of the diameter of the stumps. We soon realized, however, that this measurement was not sufficient if we wished to compute tensile strength. In later experiments, therefore, two measurements were made, one, the greater, and one, the lesser diameter of the tendon or segments; and from these the cross-sectional area of the tendon was computed as an ellipse and tensile strength computed in terms of grams per sq. Mm. In those specimens in which but one diameter was measured, the cross-sectional area was determined by assuming that the lesser diameter was slightly more than one-half of the greater. Figures on tensile strength so arrived at are recorded as *estimated*; whereas, those in which actual measurements of both diameters were made are recorded as *computed*. While we cannot claim absolute accuracy of the cross-sectional area, we believe that the error is distributed equally throughout the series and that the figures are sufficiently accurate for comparative purposes.

For purposes of study the flexor tendons were divided into a number of

groups depending upon the period of immobilization of the leg in the plaster encasement, the length of time the leg was used, and the manner in which it was used. In one group (Group B_1) observations were made on tendons taken from a leg held rigidly in a plaster encasement for periods varying from two to 35 days. In another group (Group B_2) of animals we removed the encasement after three weeks' immobilization, and the animal was allowed free use of the extremity for from one to six weeks. In a certain number of instances (Group B_3) the animal loosened or completely removed the plaster encasement. In this group, record was made of the time that this took place and the tensile strength of the sutured tendon was measured at varying intervals afterwards. In another series (Group B_4) a plaster encasement and metal splint was applied (Fig. 7) in such a manner that at the end of one week of rigid immobilization the paw was released and the animal permitted to flex but not to extend its foot beyond the point of original immobilization.

It would serve no useful purpose to report each experiment separately. Each observation is, however, recorded in the tables, and each group is separately plotted in Chart I by a curve representing the averages of tensile strength in grams per sq. Mm.

RÉSUMÉ OF PROTOCOLS OF EXPERIMENTS

Group B_1 (Table I)

Two Days.—In one of the six specimens removed on the second day (33R) the suture line held to 4 pounds at which time one of the strands of the suture broke; the other strand held to 2½ pounds and then broke. In all others the ends first separated and then the sutures pulled through the stumps. In one instance (35L) the tendon had almost the same holding power for the silk which it possessed immediately after suture, that is, 5 pounds. When pull was applied, separation started at 2 pounds, then the suture slowly pulled out of the proximal stump and separation was complete at 5¼ pounds. In the others (33L, 34L, 34R and 35R) when the pull was applied, an initial separation occurred at ¼, 2, 2, and 1 pound, respectively, and final separation took place at ¾, 3¼, 2¼ and 1¾ pounds. The tissues about the site of union at this time were soft and gelatinous. A minimal separation was observed between the tendon ends, varying from none at all to 5 Mm. in one specimen. The tensile strength in grams per sq. Mm. has been estimated for the two-day specimens at 58.19 Gm.

Three Days.—In one tendon (66L) separation began at ½ pound, in the other (67R) at ¼ pound; while final separation occurred at 4 and at ¾ pound, respectively; in each instance the suture pulled through. The tensile strength was computed at 3.55 Gm. per sq. Mm. By the third day the stumps were slightly thickened and soft, and the surrounding tissues had formed a small soft gelatinous cuff.

Five Days.—The separation started at ¾ pound in two specimens (62L and 63L), at 1½ pounds in a third (70L), and at ¼ pound in the fourth (71L). In all but one specimen (70L) the sutures pulled out of one of the stumps at ½, ¾ pound, and 1½ pounds, respectively (62L, 63L, 71L). In one specimen (70L) in which the initial separation occurred at 1½ pounds, one of the sutures broke at this pull while the other suture pulled out at 4¼ pounds carrying with it a tag of softened tendon. The computed tensile strength was 14 Gm. per sq. Mm. The stumps were possibly somewhat more edematous than on the third day; they were still gelatinous, and the intervening tissues were purplish in color.

Seven Days.—The tendon ends were becoming more definitely fused together by the cuff of soft tissue first noted on the third day. This cuff had become grayer, firmer and more fibrous in appearance. The average tensile strength (estimated) was 44 Gm. Initial separation in the seven-day specimens occurred at 1, 5/8, 3/8, 1 1/8 and 3¼ pounds, respectively. In four of the specimens the sutures pulled out of one of the stumps at 2 1/8, 1 1/8, ½ and 6½ pounds, while in one specimen (40L) the suture broke at 5 pounds after the initial separation at 2¼ pounds. We note for the first time a gelatinous layer of tissues surrounding the line of union pulling away as a definite cuff attached to one of the stumps when separation occurs.

Nine Days.—The six nine-day specimens (44L, 56R, 57R, 98L, 100L, 109R) started to separate at 1 5/8, ¾, ½, 13 1/8, 13 7/8 and 4½ pounds, respectively; in two instances (44L and 56R) final separation occurred by the suture breaking at 2½ and 5 3/8 pounds, respectively, while in all the

others the suture pulled out of one of the stumps (Fig. 2 A, B, C and D). The average tensile strength of the six specimens was 56.28 Gm. per sq. Mm. The reaction in the surrounding tissues showed no differences from those noted two days earlier except that specimens 98L, 100L and 109R were somewhat bulbous and there was moderate to marked thickening of the sheath (Fig. 3 A).

Ten Days.—The initial separation occurred at 3¾, 5½ and 5¾ pounds, while final separation in the first two specimens occurred when the sutures pulled out at 2¾ and 5½ pounds. In one specimen (87L) there was sudden separation with pull out of suture at 5¾ pounds. The tendon ends at ten days were quite intimately fused by a thick cuff of gray tissue which is part and parcel of the union (compare Fig. 2 A, B, C and D, and Fig. 3 A). Though this sheath is an important element in the tensile strength at this time, its own tensile strength is not directly proportional to its size. We may contrast here the two specimens, 86L and 87L, which broke at 5½ and 5¾

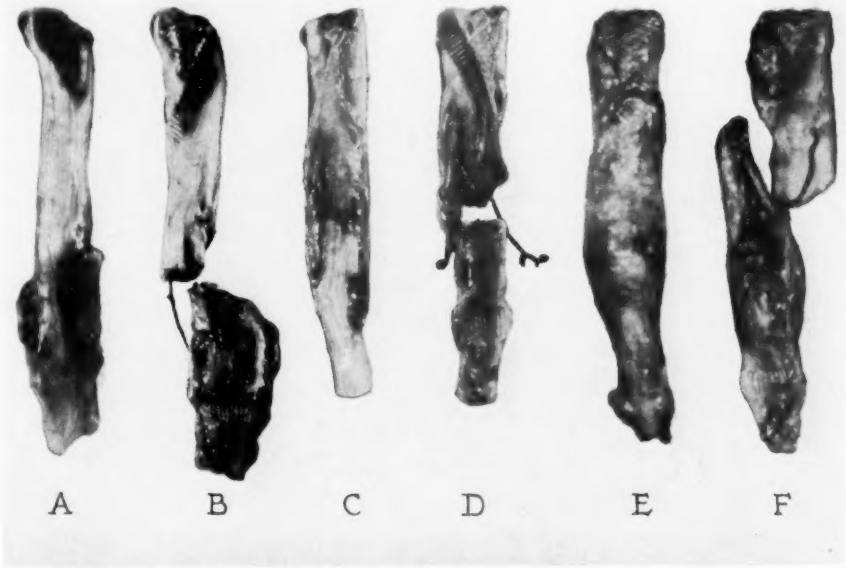

FIG. 2.—Photographs showing the manner of tendon rupture:

A and B (98L, group B_1; complete immobilization, nine days). A. Before rupture, shows bulbous thickening at site of union which is covered by a glove of thickened adherent sheath tissues with no separation. B. Rupture occurred with a pull of 6,320 Gm.; the glove remained adherent to the distal stump and the sutures pulled out of the proximal stump. Tensile strength 78.1 Gm. per sq. Mm.

C and D (109R, group B_1; complete immobilization, nine days. C. Before rupture, shows a very slight thickening. The sutures are visible through the sheath tissues. Tendon ends are visible, and there is no separation. D. Rupture occurred in a manner similar to B. Gross pull 2,042 Gm.; tensile strength 39.55 Gm.

E and F (95L, group B_1; plaster encasement, seven days, restricted use, 12 days). E. Before rupture, shows bulbous thickening. Sutures visible in gross specimen but do not show up in photograph. No separation. F. Rupture across line of union with breaking of sutures. Glove of sheath tissues remained attached to distal stump. Gross pull 5,883 Gm.; tensile strength 84.75 Gm.

pounds, respectively. The tendons in these two specimens at the time of suture each measured 8 Mm. across. When they were uncovered at the end of ten days, the site of union, that is tendon plus the surrounding tissues, measured 34.6 sq. Mm. in 86L, and 21.2 sq. Mm. in 87L. Although 86L was over 60 per cent larger, its tensile strength in grams per sq. Mm. was 61.7; whereas 87L had a tensile strength of 115.4.

Twelve Days.—The average tensile strength was 91.92 Gm. per sq. Mm. as compared with 88.55 for ten days, and ranged in the three specimens from 63.08 to 123.1. The ends of the tendons were found to be fused, and the reaction about them minimal or moderate. There was virtually no separation; in two, a questionable 1 Mm. separation had occurred; in the third, there was none. In two instances the sutures pulled out at 2½ and 3¼ pounds; in the third instance, the sutures broke at the knot at 4⅜ pounds.

Fourteen Days.—Seven specimens were removed at this stage, with the average tensile strength of 135.1 Gm. per sq. Mm. The cuff of peritendinous tissue in practically all specimens remained attached to one stump when rupture occurred through the intervening tissues; however, the sutures may either pull through or break at gross pulls of 2½ to 15¼ pounds.

Fifteen Days.—One single specimen (85R) in a very large dog broke at 4½ pounds and separated in about the same manner that one would anticipate in a nine- to ten-day specimen, with a tensile strength of but 52.9 Gm. per sq. Mm. The sheath tissues in this specimen were beginning to loosen and were slightly movable over the tendon beneath.

Sixteen Days.—Three specimens (63R, 82R, 83R) have an average tensile strength of 174.7 Gm. per sq. Mm. The cuff of surrounding tissues would appear to be adding less to the strength of union since gliding is beginning to appear. In the specimen in which this was noted (82R) the tendon fractured at the suture line at 11 pounds; then the sheath and sutures held to 6 pounds when both gave way, leaving a cuff of tissues attached to the distal stump. Separation in these three specimens was minimal—3 Mm. in 63R, and none in the other two.

Nineteen Days.—At 19 days (56L, 57L, 89R), the average tensile strength was 148.9 Gm. per sq. Mm. In one instance (56L) the separation had been 5 Mm., and the tensile strength was but 102.5 Gm. There was no separation of the stumps in the other two tendons in this group. The reaction about the site of union was not marked in any of them. The sheath tissues were gray, and the sutures could be visualized through them.

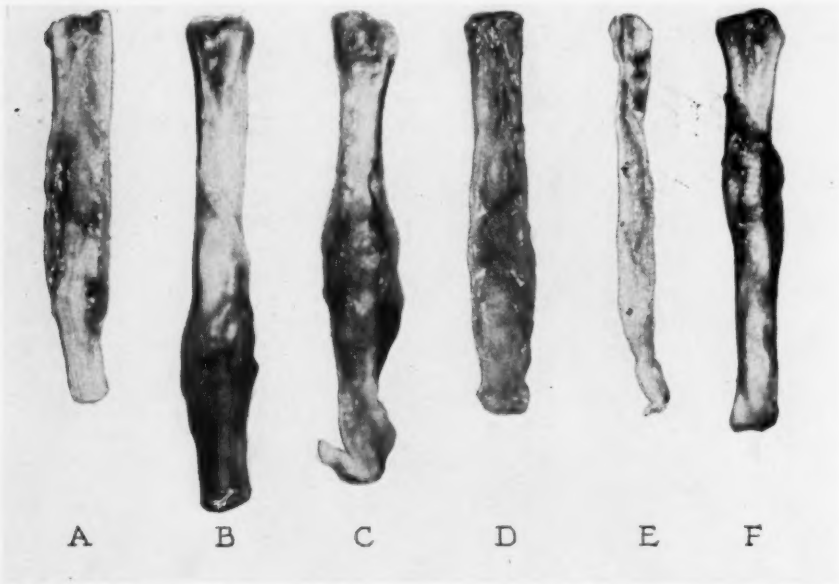

FIG. 3.—Photographs showing the types of union obtained in different flexor groups:
A (109R, group B_1; complete immobilization, nine days). Moderate reaction, moderate uniform swelling, sutures visible through sheath tissues. No separation. Tensile strength 39.55 Gm.
B (101R, group B_2; complete immobilization, three weeks, active use, two weeks). Moderate bulbous thickening. Sutures visible. Tendon glides in sheath. Ten millimeters separation. Tensile strength 377.6 Gm.
C (96L, group B_3; complete immobilization, seven days, unrestricted use, 12 days). Marked reaction and hemorrhage. Stumps bulbous. Three millimeters separation. Tensile strength 221.3 Gm.
D and E (108R, group B_3; complete immobilization, seven days, unrestricted use, nine days). Palpable bulb under skin. Each bulbous stump palpable. Sheath thick and adherent. E shows a longitudinal segment; stumps and sheath fused into continuous mass. Seven millimeters separation. Tensile strength 204 Gm.
F (106R, group B_4; complete immobilization, seven days, restricted use, 12 days). Figure 8 is drawing of this specimen. Minimal reaction in surrounding tissues. Tendon glides well through sheath. Sutures visible. Very slight enlargement of stumps. No separation. Tensile strength 176.99 Gm.

Twenty-one Days.—At 21 days (48L, 50L, 104R and 105R), the average tensile strength was 169.6 Gm. per sq. Mm. All specimens showed a minimum of reaction, and it would appear that healing was taking place under favorable conditions. All structures fractured suddenly with the application of a fair amount of gross pull, 11¾, 12, 3⅛ and 13½ pounds, respectively. The sutures and the suture line fractured simultaneously. The surrounding tissues had formed a gliding sheath and were no longer a fibrous cuff. The sutures were visible, and the ends of the tendons were not bulbous.

Twenty-eight Days.—At 28 days (95R, 96R and 100R), the tensile strength averaged 199.1 Gm. per sq. Mm. Healing has taken place very beautifully and except for a slight transverse grayish-pink or gray discoloration the line of apposition of the stumps could not be detected. There was a questionable separation of 1 Mm. in one specimen (100R), none in the other two. The sheath had completely reformed and, while slightly thicker than the normal sheath, could be lifted from the surface of the tendon to which it was attached by a few fine adhesions which allowed it to glide for 1 or 2 Mm. over the surface. The sheath was slightly grayer and less transparent than the normal sheath; however, one could see the sutures and the striated tendon beneath it. The tendon stumps, which have been enlarged in earlier specimens, were now about the same size as they had been when the suture was carried out. The manner in which 95R and 96R ruptured is of interest: In each case the rupture occurred halfway across the suture line and then, as the pull was kept up, the tendon broke across the other half at the place in the distal stump through which the tension suture had passed.

Thirty Days.—At 30 days (46R), a specimen similar in appearance to that seen at 28 days was found. The tendon ends were visible, the sutures visible, the sheath glided over the line of union, and there was no separation of the stumps. The tendon was quite small, slightly if any larger than when operation was performed. Fracture occurred across the line of apposition associated with pulling out of the tension suture on one side and breaking on the other side, at a pull of 7¼ pounds with a computed tensile strength of 267.3 Gm. per sq. Mm.

Thirty-five Days.—At 35 days (42R, 44R, 92L, 90L and 93L), the tendons had the same gross appearance that was exhibited by the 28- and 30-day specimens. The union in all looked perfect (Fig. 4); in one, a possible separation of 1 Mm. was measured; in the other four there was no apparent separation. The sheath was thin and transparent so that the sutures, including the fine appositional ones, were visible. The tendon glided through the sheath tissues without obstruction. The tendon itself was not bulbous; in fact, in two instances (42R and 44R) the diameter was slightly less than it had been at operation five weeks previously. All five ruptured through the suture line at gross pulls of 1½ to 12¾ pounds. The tensile strength varied from 61.9 to 291.5 Gm. per sq. Mm., with an average of 177.4.

FIG. 4.—(92L, group B_1; complete immobilization, five weeks.) With continuous immobilization in a plaster encasement the tendon heals with a minimum of reaction. The sutures, now lying relaxed on the surface, are visible through the thin transparent sheath which allows the tendon to glide through it. The suture line is just visible, and there is no separation. Tensile strength 291.5 Gm.

Résumé.—Group B_1: The healing process when the leg is immobilized continuously in a plaster encasement, up to and including the fifth week, presents an orderly course of events. At two days, the tensile strength is very low, though not so low as it will be on the third or fifth day, and, certainly, much lower than the holding power of the tendon for the suture. The strength of union at this time, slight as it is, is due to the suture, but this strength is lower than the tested holding power of the fresh tissues for the suture. We can assume, therefore, that the healing process in the tendon is associated with softening of the tendon. Not only are the tissues across the line of union without any effective tensile strength, but the efficiency of the sutures themselves is very much diminished by the softening. This softening is progressive for several days, and on the third and the fifth days the tensile strength is still very low, and the sutures pull through the tendon stumps. However, on the fifth day both the holding power of the tendon and the

TABLE I

RÉSUMÉ OF EXPERIMENTAL DATA. FLEXOR TENDONS, GROUP B_1

Continuous Immobilization

No. of Dog	Day	Separation of Stumps. Mm.	Manner of Separation	Gross Pull. Gm.	Tensile Strength (In Gm. per Sq. Mm.) Computed	Estimated	Average
33R	2	1.5	3	1,815.0		160.6	
33L	2	0.0	2	113.4		5.9	
34R	2	2.0	2	907.0		41.3	
34L	2	0.5	2	907.0		41.3	
35R	2	5.0	2	453.6		24.08	
35L	2	0.0	2	907.0		77.0	58.19
66L	3	0.0	2	226.8	4.19		
67L	3	0.0	2	113.0	2.92		3.55
62L	5	6.0	2	340.2	11.46		
63L	5	2.0	2	340.2	10.24		
70L	5	0.0	3	680.4	27.94		
71L	5	0.0	2	226.9	6.38		14.00
36L	7	0.0	2, 4	453.0		20.63	
37L	7	1.0	2	283.5		12.89	
38L	7	1.0	2	171.0		7.73	
39L	7	1.0	3	737.0		33.53	
40L	7	1.0	3	1,475.0		147.4	44.00
44L	9	0.0	3	737.2	32.3		
56R	9	3.0	3	340.2	22.2		
57R	9	2.0	2	226.9	10.99		
98L	9	0.0	2	6,320.0	78.1		
100L	9	1.0	2	5,981.0	152.57		
109R	9	0.0	2	2,042.0	39.55		56.28
55R	10	1.0	2	1,598.0		72.7*	
86L	10	0.5	2, 4	2,495.0	61.7		
87L	10	2.0	2, 4	2,609.0	115.4		88.55
42L	12	1.0	2	1,134.0	89.58		
43L	12	1.0	3	1,984.0	63.08		
46L	12	0.0	2	1,474.1	123.1		91.92
52R	14	0.5	3	2,609.0	102.52		
52L	14	7.0	4	2,041.0	94.19		
53R	14	1.0	3	3,686.0	163.0		
53L	14	2.0	2	1,134.0	67.5		
80L	14	0.0	2, 4	4,593.0	98.54		
81L	14	0.0	4	6,920.0	187.4		
99R	14	0.0	3, 4	4,309.0	232.9		135.1
85R	15	1.0	3	1,921.0	52.9		52.9
63R	16	3.0	4	5,443.0	260.0		
82R	16	0.0	4	5,001.0	181.2		
83R	16	0.0	3	2,041.0	83.1		174.7

TABLE I (*Continued*)

No. of Dog	Day	Separation of Stumps. Mm.	Manner of Separation	Gross Pull. Gm.	Tensile Strength (In Gm. per Sq. Mm.) Computed	Estimated	Average
56L	19	5.0	4	2,382.0	102.5		
57L	19	0.0	4	3,744.0	175.2		
89R	19	0.0	2, 4	3,061.0	169.2		148.9
48L	21	5.0	4	5,330.0	235.6		
50L	21	0.0	1	5,445.0	199.9		
104R	21	0.0	1	1,824.0	85.0		
105R	21	0.0	3, 4	6,123.0	158.2		169.6
95R	28	0.0	1	5,699.0	179.2		
96R	28	0.0	1	4,196.0	209.2		
100R	28	1.0	4	4,599.0	209.1		199.1
46R	30	0.0	2	3,402.0	267.3		267.3
42R	35	0.0	2	2,042.0	210.9		
44R	35	1.0	3	666.4	61.9		
90L	35	0.0	1, 2	2,949.0	163.0		
92L	35	0.0	1, 2	7,145.0	291.5		
93L	35	0.0	1, 2	5,670.0	160.2		177.4

Key to Manner of Separation:

1—Fracture.
2—Separation followed by suture pulling through.
3—Separation followed by suture breaking.
4—Fracture with cuff.
5—Step-cut.
NB—No break.
MTJ—Rupture at musculotendinous junction.

* Not computed in averages.
[a] Segment only tested.
The key, and these footnotes, pertain to all tables where noted.

tensile strength are beginning to rise. On the seventh day these are still further increased. Not only does initial separation require a greater pull, but the sutures may occasionally break, as they do in the fresh tendon. By the tenth day we see striking evidence of the value of the surrounding tissues which now have formed a solid cuff about the stumps. In specimens up to seven days this tissue has been soft and easily ruptured; at ten days, it presents itself as a definite entity which is adherent to the stumps and binds them together. When separation occurs, this cuff of surrounding tissue strips away from one of the stumps and remains attached to the other. The cuff has been present all along; however, in the earlier stages it has been quite soft and has usually broken irregularly or with tags at the suture line (compare Fig. 2 A, B, C and D). At 14 days, the average tensile strength is slightly higher than at 12, but the gross pull required to separate is greater, and the cuff seems here to have reached its maximum. Although the cuff

tends to revert to gliding tissue some time between the fourteenth and twenty-first day, we may occasionally find it as late as the twenty-eighth (50R) and thirty-fifth day (45R). As the cuff becomes areolar or separates from the tendon between the fourteenth and nineteenth day, the tensile strength of the tendon seems to reach a sort of plateau. From the nineteeth day on, the tensile strength rises slowly until about the twenty-first day, when it reaches a second plateau which it tends to maintain for the following two weeks provided the leg is kept immobile in the plaster. Despite a tendency for a slight rise in the curve up to the twenty-eighth day, and a marked elevation in one specimen on the twentieth day, at 35 days, the average of five reasonably consistent specimens was lower than that for three equally consistent ones at 28 days, and practically equal to that shown at 21 days. The gross appearance of tendons immobilized four to five weeks has direct practical significance. They were seen to be beautifully healed (Fig. 4); the tissues about them were transparent and areolar and glided over the surface of the tendon, and the tendon itself glided through them. At five weeks, the gross appearance was that of a definite sheath. This sheath was slightly thickened over the operative area and was continuous with the perimuscular fascia above and the peritendinous fascia below. The line of apposition in some specimens was apparent as a thin pink or grayish seam, and the sutures were seen to lie on the surface of the tendon covered by a thin transparent layer of tissue. It had the appearance of primary union.

Group B_2 (Table II)

This group is made up of animals in which the plaster encasement was removed at the end of three weeks, and the dog had free and unhampered use of his leg until the tendon was removed.

Twenty-five Days.—At 25 days (54L) (tendon immobilized 21 days and free use four days), the operative area and tendon ends were found covered by a reddish-gray tissue through which the sutures were just visible. Where the tendon ends had fused, the tissue was homogenous and gray; the line of apposition was obscured. The tensile strength of this specimen was quite high—339 Gm. per sq. Mm. The specimen fractured at 11¼ pounds through a nick which had been accidentally made in it. It was not possible to locate this nick, and computation of tensile strength was made on measurement of the entire tendon, and it seems likely that the actual tensile strength was higher.

Twenty-eight Days.—At 28 days (immobilized 21 days and free use seven days), there are three specimens (48R, 50R, 51R), two of which we were able to fracture, while one (51R) could not be broken when subjected to a pull of 37 pounds. We do not know, therefore, what the actual strength of this tendon was, although it must have been well over 300 Gm. per sq. Mm., which would have been its tensile strength had it fractured at that time. In the two tendons which were broken, fracture occurred suddenly through the line of fusion; all structures including the embedded silk broke at once. One tendon (48R) broke at 13½ pounds with tensile strength of 318.5 Gm. per sq. Mm. The other (50R), a much larger tendon, broke at 33 pounds with a tensile strength of 297.9 Gm. per sq. Mm. A cuff was still present in one case, but it does not seem to be a very important element in the union since it could be easily stripped from the tendon to which it was attached by some fine adhesions. The tendon ends themselves were slightly bulbous and gray, and the sheath tissues over them gray and almost opaque, so that measurements were difficult.

Thirty Days.—At 30 days (58L) (21 days' splinting and nine days' free use), the tendon could not be ruptured with a pull of 29 pounds. True estimate of its actual tensile strength could not be made. However, computing its strength on the assumption that it had broken, it would have been 461 Gm. per sq. Mm., which it of course surpassed. There were some fine adhesions about it; it was thicker than normal; and showed more reaction than the continuously immobilized tendons.

Thirty-five Days.—At 35 days (41R, 98R, 101R and 102R), the stumps were bulbous and the sheath tissues moderately or markedly thickened. In one instance (41R) the dog was in poor general

condition, and in this specimen the healed defect and sutures were easily seen. Rupture took place through the intervening tissues with a pull of 13¼ pounds, with a resultant tensile strength of 279.5 Gm. per sq. Mm. In another tendon (98R, Fig. 5) the union was large and bulbous, measuring 18x25 Mm. There was considerable bleeding when the subcutaneous tissues were separated from the outer layers of the sheath, and it was impossible to make the measurements. The entire specimen could not be ruptured, and two longitudinal strips were tested. The average tensile strength of these strips was 1,015 Gm. per sq. Mm. Both of the other specimens were also bulbous (Fig. 3 B) but not so markedly as 98R, and exhibited separations of 10 and 7 Mm., respectively. The manner of separation of the two differed, however. In 102R, rupture took place as a sudden fracture through the intervening tissues, while in 101R a step-cut type of rupture occurred, one-half of the tendon giving

FIG. 5.—(98R, group B_2; complete immobilization, three weeks, active use, two weeks.) Large bulbous type of union occasionally seen when unrestricted active use is instituted after three weeks' rest in a plaster encasement. All structures thick and adherent. Sutures not visible. Bulb measured 18x25 Mm. Tensile strength 1,015.0 Gm.

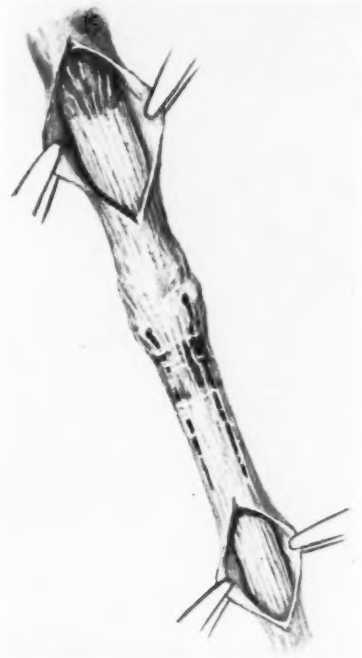

FIG. 6.—(103R, group B_3; 11 days' immobilization in a plaster encasement, ten days' unrestricted use. Dog had distemper.) A moderately bulbous union resulting from early unrestricted use after a short period of immobilization. Separation of stumps 7 Mm., but sutures lie relaxed on surface. Tensile strength 234.3 Gm.

way through the intervening tissues, the other half through the distal stump where it had been traversed by the suture.

Forty Days.—At 40 days (40R), with 21 days' rest in a plaster encasement and 19 days' unrestricted use, we have a single specimen. Here there was a local infection with marked reaction and with a sinus draining through the skin from one of the tendon sutures. The tendon, however, could not be broken with a pull of 20 pounds but rupture occurred at the musculotendinous junction. The actual tensile strength is not known since the tendon was not split to make this determination; however, its tensile strength was greater than that of the musculotendinous junction, which we estimate at approximately 321 Gm. per sq. Mm. There was here a separation of 10 Mm. between the stumps.

Forty-two Days.—At 42 days (36R, 37R, 38R, 39R) (plaster encasement for 21 days and free use for 21 days), it was not possible to rupture the new tendon with pulls ranging from 24½ to 34½ pounds. In all four specimens rupture occurred at the musculotendinous junction. We can obtain some idea as to the tensile strength of the tendon if we estimate that of the musculotendinous junction. On this basis the average tensile strength of the 42 day tendons should exceed 769 Gm. per sq. Mm. The sheath in all specimens, except that of 39R, had separated from the line of union and allowed

gliding of the tendon through it. All of the unions were bulbous, especially 39R. In this latter specimen, the sheath was fused and adherent to the tendon and to the surrounding tissues as well. There was separation of 1.5 Mm. in 38R, while 36R and 37R showed no separation.

Sixty-eight Days.—One dog was observed at the end of 68 days (43R) (26 days' immobilization in a plaster encasement and 42 days' use). Infection had taken place, and a sinus was present which had led to a knot of the tendon suture. The tendon itself was thick and edematous, as were all tissues about it. However, this thickened tendon withstood a pull of 39¾ pounds before it ruptured at the musculotendinous junction. A longitudinal segment of this tendon (after formalin fixation), with a cross-sectional area of 3.958 sq. Mm., was fractured across the line of union with a pull of 8½ pounds, with a computed tensile strength of 945.9 Gm. per sq. Mm.

TABLE II

RÉSUMÉ OF EXPERIMENTAL DATA. FLEXOR TENDONS, GROUP B_2

Continuous Plaster Encasement for Three Weeks, Then Active Use

No. of Dog	Days		Separation of Stumps Mm.	Manner of Separation	Gross Pull. Gm.	Tensile Strength (In Gm. per Sq. Mm.)		
	Plaster Case	Free				Computed	Estimated	Average
54L	21	4	?	1	6,805.0	339.0		339.0
48R	21	7	4.0	1	6,123.0	318.5		
50R	21	7	?	4	14,970.0	297.0		308.2
51R	21	7	?	NB	16,780.0			
58L	21	9	2.0	NB	13,380.0			
41R	21	14	6.0	1	6,125.0		279.5*	
98R	21	14	?	5	5,475.0[a]	1,015.0		
101R	21	14	10.0	5	6,404.0	377.6		
102R	21	14	7.0	1	3,402.0	230.4		541.0
40R	21	19	10.0	MTJ	9,071.0			
36R	21	21	0.0	MTJ	12,929.0			
37R	21	21	0.0	MTJ	14,742.0			
38R	21	21	1.5	MTJ	15,650.0			
39R	21	21	?	MTJ	11,115.0			
43R	26	42	?	MTJ	3,742.0[a]	945.9		945.9

Résumé.—Group B_2: After active, unrestricted use has been started, following 21 days' immobilization, there occurs a rapid rise in tensile strength; whereby, on the forty-second day the strength of union is greater than that of the musculotendinous junction and is estimated (on basis of our statistics) at approximately 8 per cent of the normal tendon. By the sixty-eighth day, one specimen with a computed tensile strength of 945.9 Gm. per sq. mm. had reached approximately 10 per cent of normal strength, using our average figure for normal tensile strength of dog tendon of 9,386 Gm. per sq. mm.

The cuff of surrounding tissues which began to separate during the second week becomes converted into gliding tissue which allows the underlying tendon a certain amount of motion. We do not see as thin and transparent a sheath as in the completely immobilized tendons. The tendon ends are larger and more bulbous than in the immobilized tendons (Fig. 5), and the amount of separation, where it can be measured, is greater. There seems to

be no doubt that unrestricted active use after three weeks of rest results in a marked upswing in tensile strength. The strength, however, is obtained at the expense of increase in reaction in and about the tendon as well as in a greater separation of the stumps.

Group B_3 (Table III)

In 15 instances, the dog succeeded in removing his plaster encasement completely or partially and had unrestricted use of the leg after five to 16 days of immobilization for periods of from one to 21 days. Far from being a calamity, these animals afforded us the opportunity of making some very pertinent observations. In the first place, the reaction about the site of healing was the most marked of any in the series and the average separation of the stumps was the greatest (Table VI). In one instance (84R), after 15 days of immobilization the dog, a large 65-pound animal, suddenly removed his encasement one hour before the specimen was removed, and an acute traumatic rupture occurred through the site of suture. In three dogs (60R, 88R and 58R) the amount of reaction about the operative area was so marked that measurements could be made only with difficulty, and the amount of separation could not be determined until the specimen was sectioned. There was an average separation of 5.85 Mm., or five times that seen in the completely immobilized tendons.

Twelve Days.—At 12 days (47L) (plaster encasement 11 days and unrestricted use for one day), the tendon had a tensile strength of 203.9 Gm., or double the average (91.92 Gm.) of the 12-day immobilized tendons. There was, however, a separation of 7 Mm. between the tendon ends. There was a minimum of bleeding and reaction about the operative area, but the intervening tissues between the stumps were purple in color. Rupture occurred suddenly through the intervening tissues at the suture line with 8¼ pounds of pull.

Fifteen Days.—At 15 days (84R), there was one specimen in a dog, noted above, which had removed the encasement, one hour previous to removal of the tendon. An acute traumatic rupture had occurred, the sutures were broken, the tendon frayed, and the sheath tissues had fractured.

Sixteen Days.—At 16 days (60L, immobilized nine days, and 62R, 107R and 108R, immobilized seven days), all specimens showed a maximum reaction and separation of 5 to 7 Mm. (Fig. 3 D and E). Measurements in 62R were somewhat obscured by the reaction, part of which was due to associated infection. The tendon ends in all specimens were thickened and bulbous. The tensile strength of the tendons averaged 191.55 Gm. per sq. Mm.

Nineteen Days.—At 19 days (60R, 91L, 88R and 96L), a marked rise in tensile strength was seen to have taken place. Two of the specimens (60R and 88R) could not be ruptured, by our methods, through the line of union. One (60R, immobilized five days) broke through the musculotendinous junction with 43½ pounds of pull; while the other (88R, length of immobilization not definitely known) failed to rupture with 28½ pounds of pull. A third specimen (91L, immobilized 12 days) did not fracture when 40 pounds was applied. This tendon was then split longitudinally and a small segment was tested (3.18 sq. Mm. cross-sectional area) which ruptured at 5¼ pounds, indicating a tensile strength of 749 Gm. per sq. Mm. Specimen 96L (Fig. 3 C) was markedly thickened, firm, and adherent. It withstood a pull of 25 pounds before rupturing, but because of its size had tensile strength of but 221.3 Gm. A step-cut type of rupture occurred. These specimens, as had the 16-day ones, showed a marked reaction both within and about the tendon. The ends were bulbous and gray, and the sheath about them fused to the surface and markedly thickened. Although a strong union was produced, it did so at the expense of a clean, smooth one.

Twenty-one Days.—At 21 days (51L, 77R and 103R), all three specimens showed marked to moderate reaction in the tendon ends which were gray and bulbous and were united by gray tissue grossly resembling scar. In Dog No. 51L the proliferation in and about the reactive area had obscured the sutures; measurements were difficult; and a separation of 5 Mm. was present. The tendon could not be fractured when 20 pounds of pull was applied. After the tendon had been fixed in formalin, it was split longitudinally, and three segments were tested. One segment, of which at least three-fourths was thickened sheath tissue, showed a tensile strength of 255 Gm. per sq. Mm. The two others, made up largely of tendon with small amounts of surrounding tissue, had a tensile

strength of 439.5 and 347 Gm. per sq. Mm., respectively. The average for the three segments was 347 Gm. In Dog No. 77R (immobilized seven days and unrestricted use 14 days), there was a separation of 10 Mm., resembling that constantly seen in extensor tendons. The surrounding reaction was not marked, but the ends were bulbous and many adhesions were present. This tendon ruptured with a pull of 7 pounds, with a tensile strength of 106.8 Gm. per sq. Mm. Curiously enough, separation in this specimen occurred by the sutures' pulling out intact from the distal stump. A third specimen (103R), in a dog with distemper, showed a separation of 7 Mm. (Fig. 6); it fractured partly through the suture line and partly through one stump with a pull of 12½ pounds. Its computed tensile strength was 234.3 Gm.

Thirty-three and Thirty-five Days.—At 33 days (58R, immobilized 12 days and use 21 days), and at 35 days (45R, immobilized 14 days and free 21 days), the tendons could not be broken with 16½ pounds and 26 pounds, respectively. Both showed a maximum reaction and in both the tendon ends were fused by dense, tough gray tissue.

TABLE III

RÉSUMÉ OF EXPERIMENTAL DATA. FLEXOR TENDONS, GROUP B_3

Unrestricted Use

No. of Dog	Days		Separation of Stumps Mm.	Manner of Separation	Gross Pull Gm.	Tensile Strength (In Gm. per Sq. Mm.)		
	Plaster Case	Free				Computed	Estimated	Average
47L	11	1	7.0	1	3,744.0	203.9		203.9
84R	15	1 hr.	8.0	Traumatic				
62R	7	9	5.0	1	8,844.0	216.1		
107R	7	9	7.0	1	4,763.0*	196.9		
108R	7	9	7.0	4	3,459.0*	204.0		
60L	9	7	6.0	1	6,579.0	149.3		191.55
60R	5	14	8.0	MTJ	19,735.0			
96L	7	12	3.0	5	11,340.0	221.3		
91L	12	7	6.5	1	2,382.0*	749.0		
88R	18?	1	3.5	NB	12,925.0			485.0
77R	7	14	10.0	2, 4	3,175.0	106.8		
103R	11	10	7.0	5	5,670.0	234.3		
51L	16	5	5.0		9,074.0*	347.0		229.0
58R	12	21	3.0	NB	11,790.0			
45R	14	21	4.0	NB	7,486.0			

Résumé.—Group B_3: The significant observations in this group are that unrestricted use of the tendon is reflected in the curve of tensile strength, in the amount of reaction about the site of suture, and in the amount of separation which is found between the stumps. Because of the irregular periods of immobilization and use, and the inherent variability in tendon itself, the factors are difficult to correlate. One tendon, tested on the twelfth day with but one day's use, was significantly greater in tensile strength (203.9 Gm. per sq. Mm.) than any immobilized tendon tested at that time or until the sixteenth day, at which time the average tensile strengths for three immobilized specimens and three unrestricted use specimens were about equal (174 and 192 Gm. per sq. Mm.). At 19 days the tendon with unrestricted use (91L) showed a tensile strength of 749 Gm. per sq. Mm. In contrast,

the tendons under immobilization averaged about 150 Gm. per sq. Mm. tensile strength at 19 days and 170 Gm. at 21 days. In further contrast, a tendon continuously immobilized for 30 days showed a tensile strength of but 267.3 Gm., and five tendons immobilized for 35 days had an average tensile strength of but 177.4 Gm. per sq. Mm.

The amount of reaction which is observed about the tendons in this group stands in marked contrast to that seen where rest has been provided. This is reflected in a thickening of the surrounding tissues, which may obscure

FIG. 7.

FIG. 8.

FIG. 7.—Photographs showing the method of providing for restricted use. A plaster encasement is applied from above elbow to include foot immediately after suture. Elbow and wrist held in flexion to relax the sutured tendon. At end of one week a portion of the encasement over pad of foot is cut away, allowing dog to flex foot, but extension is prevented by the aluminum splint which is incorporated in the plaster.

FIG. 8.—(106R, group B_4; complete immobilization, seven days; restricted use, in plaster encasement, as shown in Figure 7, for 12 days.) Minimal reaction about the operative area. The sheath is thin and sutures can be seen through it. The stumps are very slightly enlarged, and there has been no separation. The sutures are relaxed. Tensile strength 176.99 Gm.

the sutures, and in a bulbous enlargement of the tendon stumps (Fig. 3 C, D, E and Fig. 6). The average amount of separation is also greater where use has been allowed. Sudden unrestricted use at 15 days in a large 65-pound dog resulted in an acute traumatic rupture across the line of suture.

Group B_4 (Table IV)

In a few animals the following plan of splinting was carried out. An aluminum splint was incorporated in the initial encasement applied at time of tendon suture. At the end of one week of rigid immobilization the foot was freed and the dog permitted to flex it (Fig. 7). The aluminum splint prevented extension beyond the point at which it was originally immobilized. In a few animals, the encasement was removed under anesthesia and a fresh

one applied which fulfilled the same requirements, *i.e.*, allowed flexion but prevented extension beyond the angle at which the leg had been originally fixed. Tendons from these dogs were removed at intervals of 14, 16, 19, and 21 days following suture.

Fourteen Days.—At 14 days (72R, 73R, 74R and 76R), the line of union was visible in three of the specimens but obscured in the fourth (72R) by marked, grayish hemorrhagic tissue. This reaction, also present but in lesser degree in the other three specimens, had produced a thicker cuff than seen in the immobilized specimens. The tendon ends also had taken part in this reaction and were slightly thickened. In two specimens (73R and 74R) there was no separation at the suture line, while in one (76R) a separation of 3 Mm. was found. In two specimens (72R and 73R) when a pull was applied the stumps separated and the sutures pulled out at 8½ and 3 pounds, respectively. In 74R separation started at 9½ and was complete at 11 pounds with breaking of the suture. In 73R simultaneous separation of the intervening tissue and sutures occurred at 10 pounds. The average tensile strength for the four specimens was 125.6 Gm. per sq. Mm., approximately the same as for dogs completely immobilized for the same period of time.

Sixteen Days.—At 16 days (75R) with seven days' rigid immobilization and nine days' restricted use, the appearance of the union was good. The ends were fused in a gray cuff of tissue and there was but slight bleeding when the tendon was uncovered. It was somewhat difficult to measure the amount of separation, but it appeared to be about 2 Mm. The tendon ruptured with a gross pull of 15 pounds and exhibited a tensile strength of 295 Gm. per sq. Mm. Separation occurred when the intervening tissue fractured, and the sutures broke. The cuff of surrounding tissues remained attached to the distal stump (compare Fig. 2 F).

Nineteen Days.—Two quite disconcerting specimens were encountered at 19 days (106R—Fig. 3 F and Fig. 8; and 95L—Fig. 2 E), in that computations for tensile strength gave such divergent results and were much lower than had been anticipated from the preceding and succeeding specimens. Dog No. 106R presented a very satisfactory picture of healing by primary intention. The stumps were only slightly enlarged, there was a thin movable sheath which allowed the underlying tendon to glide beneath it, and all sutures including the fine approximating sutures were clearly visible.

It ruptured by fracture through the suture line with a pull of 12⅜ pounds and had a computed tensile strength of 176.99 Gm. per sq. Mm. Dog No. 95L also exhibited but moderate thickening of the stumps. However, the tendon glided rather poorly through the sheath. The sheath itself was thick and adherent to the tendon and surrounding tissues. Separation occurred with a pull of 12⅛ pounds. The heavy sheath brought the cross-sectional area of this tendon up to a figure approximately that of a human Achilles tendon. Rupture in both of these specimens (Fig. 2 E and F) occurred through the suture line, the proximal stump pulling away from the distal, leaving the thickened sheath attached to the distal stump. The thick sheath added to the cross-sectional area but contributed very little to tensile strength.

Twenty-one Days.—At 21 days (78R), the tendon was seen to be firmly united by a thin line of gray tissue 1 Mm. wide. The sheath was gray but transparent and glided over the surface. Separation of the stumps occurred by sudden step-cut fracture at 15½ pounds, with a tensile strength of 699.3 Gm. per sq. Mm.

TABLE IV

RÉSUMÉ OF EXPERIMENTAL DATA. FLEXOR TENDONS, GROUP B_4

Restricted Use

No. of Dog	Days: Plaster Case	Days: Use	Separation of Stumps Mm.	Manner of Separation	Gross Pull Gm.	Tensile Strength (In Gm. per Sq. Mm.): Computed	Estimated	Average
72R	7	7	?	2	3,856.0		119.0*	
73R	7	7	0	2	1,376.9	53.71		
74R	7	7	0	1, 4	4,309.0	130.62		
76R	7	7	3	4	4,536.0	192.6		125.6
75R	7	9	2	1, 4	6,803.0	295.0		295.0
95L	7	12	0	1, 4	5,883.0	84.75		
106R	7	12	0	1, 4	5,614.0	176.99		130.8
78R	7	14	1	1	7,003.0	699.3		699.3

Résumé.—Group B_4: The reaction at the site of operation and the amount of separation were less in these tendons with restricted use than in those which had had uncontrolled use before the three-week period had ended. However, the reaction was more marked than had been observed in dogs under complete immobilization. The amount of separation, however, was less than in the completely immobilized group (Table VI). At two weeks, when the first observation was made, the average tensile strength was practically the same as that for completely immobilized dogs. The manner of separation of the stumps at the time of rupture was also the same as that of completely immobilized tendons; that is, the stumps separated through the intervening tissue leaving a cuff of proliferated surrounding tissue attached to one of them.

Two specimens, one at 16 days and one at 21 days, had high tensile strengths. In the case of the 16-day specimen (75R), which separated with a cuff, 15 pounds' pull was required to rupture it, with a tensile strength of 295 Gm. per sq. Mm. This is somewhat higher, but not greatly so, than the highest of the three 16-day specimens with complete immobilization. The 21-day specimen (78R) presented a fine, clean-looking union with 1 Mm. separation; a minimal reaction; and covered by a gliding sheath. It required 15½ pounds to rupture it, and it was computed to have a tensile strength of 699 Gm. per sq. Mm. The tendon ruptured, however, not at the suture line but at a place where the tendon was traversed by the silk. While this figure of 699 Gm. per sq. Mm. is a single one, it is much higher than any of the 21-day specimens which were completely immobilized and even higher than a 25-day specimen with three weeks' immobilization and 4 days' use.

Two 19-day tendons, however, had the same tensile strength that was shown by completely immobilized tendons of the same age. It seems quite evident that function has influenced the tensile strength curve but that the effect is manifested only in the third phase of healing, *i.e.*, during the second period of increase of tensile strength.

Extensor Tendons (Table V)

Sixteen extensor tendons were sutured and examined at intervals of 2, 14, 21 and 42 days. The series is quite small, and our calculations as to tensile strength in all of them have been based upon an estimated cross-sectional area derived from a measurement of the width of the tendon at time of removal. However, in the course of our experimental studies during the past few years, several hundred extensor tendons have been operated upon, and while tensile strength figures are lacking in these, our general observations in this larger group substantiate the findings made in the present smaller series.

Two Days.—At two days after suture (25R and L, 26R and L, 29R and L, 30R and L), three specimens (25L, 29L and 30L) exhibited no evidence of union, while in the other five, despite wide separation, the ends were held together by a soft, gelatinous hemorrhagic clot. The reaction about the site of union was quite marked especially when compared with two-day specimens in the flexor series. There was marked separation of the stumps at the suture line, a phenomenon which seems to occur, almost invariably, following suture of this tendon. We have not been able to overcome this separation by any methods of suture so far tried. It has been less with the type of suture here described than with any other thus far used. We cannot say whether this is a phenomenon of extensor tendons in general or is due to our inability to immobilize the dog's foot adequately. At two days, the separation varied from 12 to 20 Mm., and averaged 15 Mm. The sutures, with this amount of separation, have, of course, either broken (29R) or pulled partially or completely (25R and L, 29L) through one or other of the stumps. In one instance (30R) the sutures had pulled partially through both stumps and in doing so had pulled a core of tendon from the center of the proximal stump. Very little holding power of the sutures is manifest. The initial separation occurred at an average gross pull of 201 Gm. Separation of stumps with pull-out of sutures occurred in three instances (26R, 30R, 30L) at 2 pounds 3 ounces, 2½ pounds, and 1 pound, respectively. The suture-holding power of the tendon is very low, even lower than in the flexor group. At two days, the average holding power of the tissue for the suture in the flexors was 3 pounds 2 ounces; whereas, in the extensors it was 1 pound 1 ounce. Initial separation of the stumps in the flexors occurred at 1 pound 14 ounces; in the extensors it averaged just under 6 ounces.

Fourteen Days.—At 14 days (31L), the stumps were united by a reddish-gray tissue through which the sutures were still visible. There was a separation of 18 Mm., but the sutures had not pulled completely out of the stumps and were held moderately firmly. Fracture through the intervening tissue occurred suddenly at 6½ pounds with simultaneous fracture of one suture and of intervening tissue. At the same time the other suture pulled out of the distal stump intact. The tensile strength of this specimen we have estimated at 129.8 Gm. per sq. Mm.

Twenty-one Days.—At 21 days (27L, 28L, 32L), the separation between the stumps was 17, 34 and 26 Mm., respectively. Despite this amount of separation and the great amount of reaction present, the tendons functioned well; that is, when the other extensor tendons were divided, pull upon the sutured extensor carpi radialis extended the paw to 180°. Rupture occurred in three different manners in the specimens and at quite different amounts of gross pull. In one (27L), the sutures pulled out of the distal stump at 2¾ pounds, bringing with them a small fragment of the stump. In another (28L), sudden fracture of the intervening tissue and the suture occurred at 10½ pounds. In the third (32L), sudden fracture through the intervening tissues occurred at 17½ pounds, but this time the frayed, red, thick distal stump pulled away from the proximal stump as if from a socket formed by the thickened sheath tissues. Despite the great difference in gross tensile strength the estimated strength of the three was but 105.9, 151.6 and 168.1 Gm. per sq. Mm., with an average of 141.8. The average separation of the three 21-day specimens was 25.6 Mm.—almost double that of the two-day specimens.

Forty-two Days.—At 42 days (27R, 28R, 31R and 32R), strong tendons had developed except in one specimen (28R), in which the sutures had pulled out and there was no union at all. The separation for the four tendons including the one in which no union had occurred was 34 Mm.; however, in one instance there was but 10 Mm., while in the others it was 45, 50 and 30 Mm. The reaction in the specimen showing but 10 Mm. separation was very minimal, the stumps were only slightly bulbous and appeared continuous with the intervening tissues. This tendon glided well and extended the forepaw to 180°. When subjected to 40 pounds of pull it ruptured through the musculotendinous junction, and when retested it slipped out of the forceps at 53 pounds. Estimated tensile strength based on this latter figure would exceed 1,276 Gm. per sq. Mm. The other two tendons ruptured through the intervening tissues, one at 25 pounds of pull, the other at 20 pounds. The amount of reaction about the operative area, however, produced a thick, heavy mass of tissue which, while able to withstand considerable gross pull, possessed very low tensile strength per sq. Mm.—240.5 and 110 Gm. (estimated), respectively.

Résumé.—Extensor Tendons: Healing in the case of the extensor tendons occurs despite the great amount of separation which obtains. This separation appears to be progressive in nature and is greater at six weeks than at three weeks or at two days. The holding power of the tendon for the sutures diminished more rapidly in the case of the extensors than the flexors and at two days is only about one-fifth of that which was present immediately after the suture. Even at 21 days, suture pull-out may occur. Our observations

seem to indicate that the curve of wound healing in the case of the extensors resembles that of the flexors but that it progresses at a slower pace.

Discussion.—The curve of healing for sutured tendons, as measured by return in tensile strength, appears to be similar to that for healing in other tissues. However, the process, when observed beyond the stage of fibroplasia, seems to respond or react in a definite manner to functional demands put upon it. If we take as a gauge simply the return of tensile strength, we are apt to ignore certain other effects of motion upon the healing process, the disadvantages of which may far outweigh the advantages of a rapid increase in strength. There is no doubt but that we have in function a valuable aid

TABLE V

RÉSUMÉ OF EXPERIMENTAL DATA. EXTENSOR TENDONS

No. of Dog	Day	Separation of Stumps Mm.	Manner of Separation	Gross Pull Gm.	Tensile Strength (In Gm. per Sq. Mm.) Computed	Estimated	Average
25R	2	12	1	28.35		1.71	
25L	2	15	No union				
26R	2	13	2	56.7		4.81	
26L	2	13	2	696.5		44.95	
29R	2	15	2	113.4		5.19	
29L	2	20	No union				
30L	2	17	No union				
30R	2	16	2	113.4		9.63	13.25
31L	14	18	2	2,835.0		129.8	129.8
27L	21	17	2	1,247.0		105.9	
28L	21	34	1	4,763.0		151.6	
32L	21	26	2	7,940.0		168.1	141.8
27R	42	10	NB	24,005.0			
28R	42	45	No union				
31R	42	50	1	11,340.0		240.5	
32R	42	30	1	9,071.0		110.0	175.0

in healing, but it remains to be determined how and when to make use of it.

The answer as to when function is effective in the healing process of tendon may be suggested by a study of the curves of tensile strength of the various groups of tendons (Chart 1).

During the first four or five days after suture the gross tensile strength of the sutured tendon drops to considerably less than that found to be present immediately following operation. During this time the ends become soft and are held together by a gelatinous exudate, which possesses a very minimum of tensile strength. Along with this, the softened stumps have considerably less holding power for the sutures than was present when they were intro-

duced, and when stress is applied the sutures instead of breaking simply pull out. Beginning about the fifth day there is noted an increase in tensile strength which continues until the fourteenth to sixteenth day when the strength in most specimens seems to have reached a plateau where it remains until about the nineteenth day, when a second plateau is reached about the twenty-first day, and this is maintained for the next two weeks. Whether or not we are dealing simply with a delay in healing, *i.e.*, in the progress of

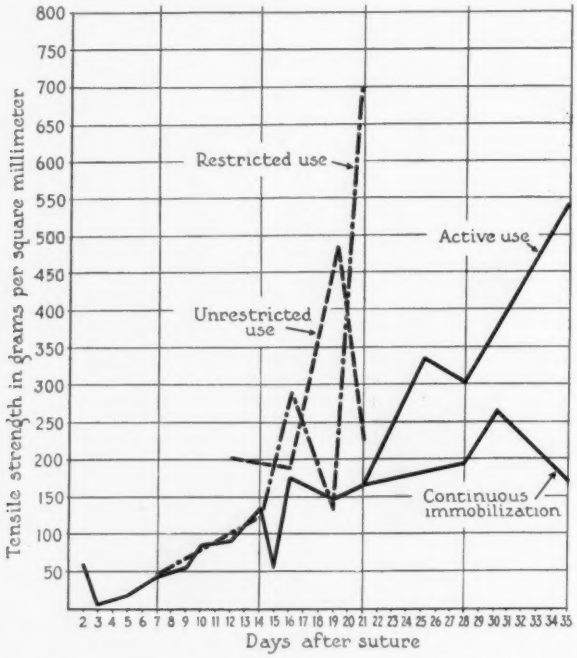

CHART 1.—Tensile strength in grams per sq. Mm. of healing flexor tendons from two to 35 days following suture. The lower, continuous curve, group B_1, represents tendons continuously immobilized. The curve for group B_2 represents tendons immobilized for three weeks and then subjected to immediate active use; it branches off of the group B_1 curve on the twenty-first day. Tensile strength values for tendons subjected to either unrestricted or restricted use, groups B_3 and B_4, are plotted up to 21 days only.

differentiation, we cannot say since our observations on continuous immobilization do not extend beyond the 35-day period. It may be that despite immobilization the tensile strength will slowly approach that of normal tendon; however, the rather consistently lower figures for tensile strength obtained at five weeks suggest that the line of union may show atrophy of disuse. Disuse may be a more important factor in tendon healing than studies based on histologic sections seem to indicate. Immobilization in a plaster encasement, however, does not put the muscle entirely at rest; tension and tonic pull are undoubtedly present, and these factors must act upon the healing tendon as a functional stimulus.

When there is introduced into the process function and tension greater than that afforded by muscle tone and the motion possible with splinting, the curve of healing is changed; and the tensile strength mounts more rapidly. This is evident if we compare the curve of the tensile strength values obtained in tendons allowed unrestricted use after three weeks in a cast. It rises sharply from the plateau of about 200 Gm. per sq. Mm., and at the end of one week of use is already 50 per cent stronger than immobilized tendons of the same age. We do not believe that this finding is due simply to the great variability of tendon tissue since the same tendency to more acceleration of the curve is also evident in the two other groups of animals in which a functional stimulus was present.

In those instances in which the encasement was removed by the animal, and free, unrestricted use was started earlier than three weeks, the same tendency to abrupt rise in tensile strength is noted. However, it is important to note that this rise in tensile strength does not occur until a certain stage in healing has been attained. At 16 days, both the mobilized and the immobilized tendons have approximately the same average tensile strength. At 19 days, however, the used tendons are very strong in comparison with immobilized ones. This rise manifested at 19 days has not been observed in the 21-day specimens, and there would appear to be a contradiction present. The group of animals here concerned had removed their encasements and had used the operated leg without restriction; so that while we have the element of function entering in, it has consisted of violent use. It is of interest to note that the amount of separation in the three 21-day tendons varies inversely with their tensile strength. Thus, the tendon with but 5 Mm. separation had tensile strength of 347 Gm. per sq. Mm.; that with 7 Mm. separation had a tensile strength of 234.3 Gm.; while that with 10 Mm. separation had a tensile strength of but 106.8 Gm. The number of days which the tendons had been immobilized varied directly with the tensile strength; with 16 days' immobilization the strength was 347, with 11 days, 234.3, and with seven days, 106.8. No definite conclusions are permissible, but the findings are suggestive, and the general tendency for these tendons to arrive at very high tensile strengths seems to us evident.

Similar observations were made upon the group of dogs which were allowed restricted motion after one week of rigid immobilization. Four specimens, examined at 14 days, showed a tensile strength the same as that for the immobilized dogs. At 16 days, and especially at 21 days, however, the strength was well above that for the immobilized specimens. In these animals function in the form of flexion of 10° to 15° had been permitted from the seventh day after operation. However, it had produced no change in tensile strength up to 14 days. After this time, however, the tensile strength curve while inconsistent is different from that of the completely immobilized group. The drop at 19 days in the restricted tendons and at 21 days in the unrestricted ones cannot be explained. However, the fact remains that the only

tendons which attained high levels of tensile strength during the five-week period of observation were those in which a functional stimulus was present.

There are, of course, many other factors which have to do with healing besides that of function; in fact, it is commonly conceded and has been abundantly illustrated that rest and quiet are necessary for good wound healing and that motion and activity retard the process. We must inquire, therefore, if there is a certain phase in the healing process of such a structure as tendon

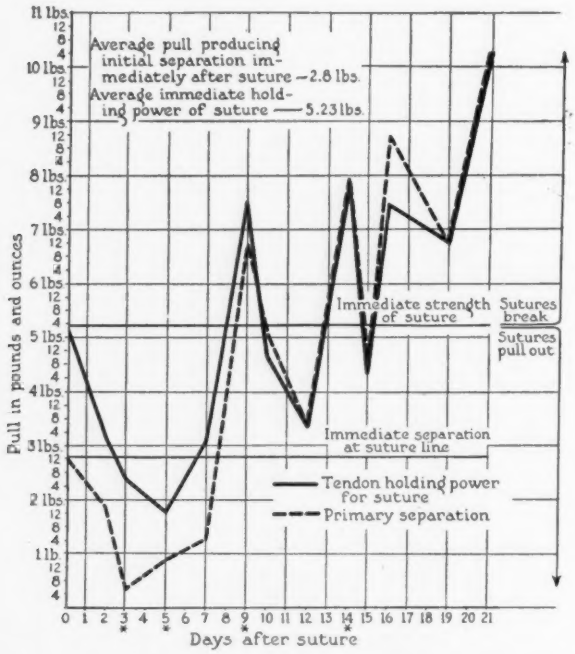
Average pull producing initial separation immediately after suture —2.8 lbs.
Average immediate holding power of suture —5.23 lbs.
Immediate strength of suture
Sutures break
Sutures pull out
Immediate separation at suture line
Tendon holding power for suture
Primary separation
Pull in pounds and ounces
Days after suture

CHART 2.—Showing the holding power of tendon for suture and tensile strength of sutured tendon in pounds per tendon.

when use and motion are actually harmful and another phase when they may be beneficial. We should know, also, whether this marked increase in tensile strength may not be obtained at the expense of other more important desiderata.

If we compare the curves for tensile strength of the completely immobilized tendons with the curves for restricted and unrestricted motion, it is seen that at the 14- and 16-day period of observation the same tensile strength was present in all three groups. After 14 to 16 days we see, however, that the tensile strength increases more rapidly in those tendons which had been subjected to some degree of function. It would seem logical to conclude, therefore, that function has very little effect upon tensile strength of the union previous to the fourteenth or sixteenth day. Our observations indicate, therefore, that, granted that function were a valuable aid to the

healing of tendons, so far as tensile strength is concerned it does not exert its influence before approximately two weeks after suture. The tendon kept completely immobile for two weeks, that with a limited period of rest and unrestricted use, and that with restricted use arrive at the 14-day stage with about the same tensile strength. Function exerts its influence during the second phase of increase in strength, the period of maturation or organizing differentiation of the tendon. This starts, as previous histologic studies have shown, about the fourteenth to sixteenth day, and is manifested in tensile strength experiments by a tendency for the curves of all tendons to begin to rise after the sixteenth day.

The holding power of the tissues for the suture is also of significance here and has a direct bearing upon the problem as to when motion should be started. In Chart 2 are plotted two curves. One curve represents the amount of pull in pounds required to produce initial separation of the sutured tendon ends. Size of tendon and cross-sectional area are not taken into consideration. The other curve represents the amount of pull in pounds necessary to pull the suture out of the tendon or to break the suture. To arrive at base lines for this chart, a number of tendons were sutured with No. 8 Champion, twisted, untreated silk and were immediately subjected to pull. At an average pull of 2.8 pounds the tendon ends began to separate slightly, and at an average pull of 5.23 pounds separated completely. Separation occurred in every instance by the sutures breaking at the knot. Lines are drawn across the chart at the level of 2.8 and 5.23 pounds and represent the immediate strength of a sutured tendon.

As Howes has shown for fascia, the immediate strength of the sutured tendon depends upon the functionating strength of the suture. It is evident that we are not taking advantage of the entire holding power of the tendon and that a heavier suture would be necessary to do so. We have not tried to determine the ultimate holding power with our method of suturing since as far as our present work is concerned, this would necessitate the use of heavier sutures. As a matter of fact, the suture we have used is heavier than necessary as may be noted in Chart 2.

During the first ten to 14 days after operation the sutured tendon separates in a consistent manner. As pull is exerted upon the stumps, separation first occurs across the line of union but the stumps are still held together by the suture. With increasing pull the sutures give way by pulling through the stumps and separation is complete. Following the fourteenth day, separation of the stumps is usually associated with a breaking of the sutures. There is an occasional pulling-out of the sutures after 14 days, and an occasional breaking of the sutures before 14 days, but the variations are no greater than would be expected.

Examination of Chart 2 shows that both the curve for primary separation and that for tendon holding power drop precipitously. The curve for primary separation which really represents tensile strength of the union

falls on the second day to under 2 pounds and on the third day to about 6 ounces. On the fifth day the tensile strength has started to rise and by the ninth day crosses its theoretic base line below which it does not subsequently drop. The curve for tendon holding power for the sutures starts at 5.2 pounds, but by the second postoperative day has dropped to slightly over 3 pounds. This actually represents holding power since final separation occurs not by fracturing, as obtains immediately after suture, but by the sutures' pulling out of the stumps. This curve drops to its lowest level on the fifth postoperative day, a time which coincides with the period when fibroplasia and tendon proliferation begin. After the fifth day the holding power mounts but it does not cross the base line of 5.2 pounds until some time between the twelfth and fourteenth days. After this time, although there is an occasional suture pull-out, fracture of the union is usually associated with breaking of the sutures. Chart 2 is based entirely on tendons immobilized for from two to 21 days.

These observations indicate not only that the tensile strength of a sutured tendon is extremely low for a number of days but also that the holding power of the tendon tissues drops just as rapidly. We cannot rely upon the line of union possessing the strength immediately afforded by suturing but must reckon with a significant drop in this strength. We agree with Howes that "the loss of strength of a wound was not caused by the loss of tensile strength of the suture material alone but rather by the change of all the factors which determine the strength of the wound during the latent period." We realize that moisture and exposure to tissues tend to lower the tensile strength of silk, factors which have been recently stressed by Shambaugh, and Meade and Ochsner. However, it is our feeling that the significant loss in strength in union in sutured tendon is not due to weakening of the suture itself but to softening of the tissues and diminution in holding power for the suture which occur in the early stages of wound healing. It would seem unwise to initiate function during the time both tensile strength and holding power are dropping, and quite hazardous to allow pull of any magnitude before the tendon has regained its suture holding power. So far as strength of union is concerned, the data derived from holding power of sutures and gross tensile strength of union would indicate that use should not be allowed before the tenth day and probably not before the fourteenth day.

The observations on tensile strength following suture of the extensor tendons suggest that they regain their strength more slowly than do the flexors. It seems logical to assume that this retardation in the curve is in some way associated with the separation which is invariably present between the stumps of sutured extensor tendons. This is borne out by the fact that the separation is progressive. At two days, the average separation of the extensors is 15 Mm., at three weeks, it is 25.6 Mm., and at six weeks, it is 34 Mm. Of the four six-week specimens there was one with a separation of but 10 Mm., and this was firmly healed with a minimum reaction. Its

tensile strength was greater than that of its musculotendinous junction. The other three specimens had separated 30, 45 and 50 Mm., respectively. One had not united, and the other two had healed with marked reaction. These latter tendons ruptured through the tissue intervening between the stumps at estimated tensile strength of but 110 and 240 Gm. per sq. Mm. The evidence points to the fact that a large gap gains strength slowly and is liable to stretch for a long period of time.

It is instructive to compare the amount of separation which occurs during healing in the four groups of flexor tendons (Table VI). In Group B_1, in which complete immobilization has been maintained during the whole period of observation, separation of the stumps was usually less than 1 Mm., and the average for all specimens was 1.07 Mm. When active use is begun after three weeks' immobilization (Group B_2) the amount of separation increases so that it averages 4.44 Mm. In those animals that removed their plaster encasements and used their legs without restriction earlier than three weeks after operation (Group B_3), the separation averaged 5.85 Mm. The ob-

TABLE VI

SEPARATION, IN MILLIMETERS, BETWEEN TENDON STUMPS; CLASSIFIED ACCORDING TO GROUP AND DAYS FOLLOWING SUTURE

	Days after Suture						Average Separation
Group	2	7	14	21	35	42	Mm.
Flexor B_1	1.5	1.23	1.15	1.2	0.2		1.07
B_2					5.7	2.9	4.44
B_3			7.0	5.66	4.0		5.85
B_4			1.0	0.75			0.85
Extensor	15.1		18.0	25.6		33.8	21.3

servations suggest that, regardless of the minimal amount of separation, unrestricted use, even after three weeks of complete rest, results in some further separation. It we compare with these three groups of tendons our small series of animals in which restricted motion was permitted (Group B_4), we find, here, not only very strong tendons but a minimum of separation. Here, the average separation was 0.85 Mm., slightly less than that in the completely immobilized dogs. Further observations are needed in the case of the tendons with restricted use, and it remains to be seen whether they will continue to exhibit less tendency to stretch after three or more weeks. The results to date seem to indicate that the intervening tissue between the stumps is stronger and more resistant to stretching at the end of three weeks with restricted use than in those tendons which have been kept completely immobile for a similar period of time.

The amount of reaction about the site of suture varies with the time of

onset and nature of functional use. During the early stages of repair there is, of course, a great increase in the circulation in and about the tendon; the subcutaneous tissues and the peritendinous tissues become edematous and vascular, and the whole operative area is fused into an easily bleeding soft gelatinous mass. The effect of motion on this early stage is demonstrated particularly well in the extensor tendons where marked separation and bulbous thickening of the stumps seems to be characteristic of the manner of healing of these tendons. Such reactions, however, are noted in the flexor series where active motion comes into play (Fig. 3 B, C, D, E and Figs. 5, 6 and 8). One can usually judge the degree of activity by the appearance of the stumps. Where the tendon has been completely at rest all reactions are reduced to a minimum. When such tendons are uncovered at the end of four or five weeks, the site of union is covered by a thin transparent sheath beneath which all sutures are visible (Fig. 4). The narrow line of apposition of the stumps may be just visible as a grayish or pinkish seam. The tendon itself is only slightly if any larger than when operation was performed and has regained entirely the mother-of-pearl sheen which it loses to some extent during the early stages. Where restricted motion has been permitted, there is some increase in the thickening of the sheath, the ends of the tendons are thickened for a slightly longer period of time, but the tendon and sheath tissues usually separate easily from the tendon after the nineteenth day (Figs. 3 F and 8). Active unrestricted use, however, even after a full three weeks of complete immobilization (Figs. 3 B and 5), leads to bulbous proliferation at the site of union, and afterwards to fibrous adhesions between the stumps, sheath, and surrounding tissues. Such marked reaction, as shown in Figure 5, does not always occur, but it happens with sufficient frequency that there is no question but that active unrestricted use is accountable. At times even where active use has started quite early, the amount of reaction is only moderate (Fig. 6); however, we notice in these tendons the almost invariable presence of separation (Fig. 3 D and E).

The observations made on this series of tendons would seem to show that peritendinous adhesions and reaction are definitely related to use. Excessive activity even after an immobilization of three weeks may convert a clean union into a bulbous adherent mass and cause increase of separation at the line of union. We cannot say definitely from our experimental data, thus far, whether or not unrestricted use after five weeks of immobilization would lead to stretching at the suture line, but the indications are that it would do so. Our results seem to show, however, that restricted use, while it leads to somewhat more reaction than occurs with complete rest, still does not lead to excessive reaction or cause separation. In all our animals with restricted use the period of initial complete immobilization was but seven days, and our series has not extended beyond a period of three weeks. They might also exhibit bulbous enlargements and stretching if active use were permitted after 21 days. Since, however, the tendons in this group tend to be some-

what stronger than immobilized tendons, it is not unlikely that because of increased tensile strength they would be better able to withstand functional demands.

Motion is started early following tendon repair because of the fear that binding adhesions will develop. We feel that unrestricted use must be instituted late in the process and should always be preceded by active, guarded motion. Too early use of any sort is liable to lead to marked reaction and thickening which may defeat the very purpose for which it is instituted. Gliding of the healing tendon we have observed to appear in the natural course of events of the healing process. Tendons kept completely immobilized develop excellent gliding sheaths. Too early activity will not insure gliding but on the contrary will lead to increased reaction. Similarly unrestricted use even after long immobilization may cause enlargement of the tendons, stretching of the line of union and adhesions.

SUMMARY.—A series of experiments has been carried out on the manner of healing of sutured tendons. Observations have been made on the rate of increase in tensile strength, on the effect of function on this rate of increase and on other phases of healing, and on the holding power of the tendon for sutures.

The curve for increase in tensile strength conforms to similar curves for other tissues, in that following an initial drop there is a rapid increase in tensile strength which reaches a plateau between the fourteenth and sixteenth day. This level is maintained for several days in the completely immobilized tendon until about the nineteenth day, when a slight rise occurs and a second plateau is reached which is maintained for the next two weeks. In those instances in which the plaster encasement was removed at the end of 21 days and active use of the extremity permitted, the tensile strength showed a marked rise in value over that of the immobilized specimens. In instances in which unrestricted active use of the extremity occurred earlier than the third week of healing, the tensile strength values tended to rise significantly above those of the immobilized tendons. Similar higher values for tensile strength were found in animals in which restricted or guarded use of the sutured tendon was permitted from the seventh postoperative day on. However, in these latter two groups the effect of function is not manifest until after the fourteenth day and the evidence seems to favor the conclusion that function leads to an acceleration of the phase of maturation.

Observations on the holding power of tendon for sutures have shown that, with our method of suturing and with the size of silk suture employed, the immediate strength of the suture line depends upon the strength of the silk. Immediately following suture, the union withstands a pull of 5.23 pounds before the silk ruptures and separation occurs. The holding power of the tendon for the suture is greater than the strength of the suture material used. However, this holding power rapidly and progressively diminishes and by the second postoperative day the sutures pull out of the tendon. The holding power

reaches its lowest level on the fifth day, after which it rises above the level of the strength of the suture. This rise is not consistently maintained, however, until after the fourteenth day. The tensile strength of the union, which also drops, reaches its lowest level on the third day, and by the fifth day is already on the increase. By the ninth day the tensile strength of the union approaches the holding power of the tissues for the suture. Following the ninth day the two curves are practically identical; that is, the separation of the stumps and giving way of sutures usually occur simultaneously.

The amount of separation between the tendon stumps varies directly with the amount and type of function to which the union is subjected. The least amount of separation occurred in flexor tendons which were completely immobilized or completely immobilized for one week and allowed restricted use thereafter. The greatest amount of separation was observed in those tendons which were subjected to early active use and in the extensors.

The degree of reaction about the sutured area also varied directly with the amount and type of function to which the tendon had been subjected.

It is interesting to note that the sequence of events of tendon healing follows a definite chronologic order, whether these observations are made on functional return (Stewart), metabolic changes (Gaza, Gerlach and Gissel), or from the standpoint of histology or return in tensile strength.

CONCLUSIONS

(1) Tendon healing as measured by its tensile strength exhibits three phases:

A. Phase of rapid diminution, which lasts about five days.

B. Phase of increase in tensile strength up to a plateau, which it reaches about the sixteenth day.

C. Second phase of increase in tensile strength, which probably starts between the nineteenth and twenty-first day and continues for an undetermined period of time.

(2) Curves of tensile strength conform to phases observed in histologic process of repair:

A. Phase of exudation and fibrinous union.

B. Phase of fibroplasia.

C. Phase of maturation or organizing differentiation.

(3) Function to which the healing tendon is subjected is directly reflected in the curve of the third phase of healing. During the first and second phases it produces no effect unless it is so great as to cause marked separation. During the third phase of healing function accelerates the curve.

(4) Function and motion during the first two phases of healing lead to increased reaction and to separation at the suture line. Restricted use of the tendon, started on about the fourteenth day and continued for one week, or preferably two, may be expected to lead to only a slight increase in reaction and to a rapid increase in tensile strength of the union. Active unguarded

use even after three weeks of immobilization may be associated with stretching of the suture line and always leads to increase in reaction.

(5) The holding power of tendon for the suture shows a marked drop below its original power and does not begin to rise until the fifth day after suture. It does not rise consistently above the strength of the sutures until the fourteenth day. Although the strength of union for the first nine days is essentially due to the suture, it is not so great as the immediate sutured strength until after 14 days. The importance of adequate relaxation during this time is evident.

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DISCUSSION.—DR. SAMUEL C. HARVEY (New Haven, Conn.): I am delighted to have the opportunity to discuss this most excellent paper that has been presented by Doctor Mason. It has the two aspects that are necessary, I think, to satisfy this audience whatever their interests may be. One is the theoretic aspect of wound healing and the other is the practical application of it. I should like to discuss both points briefly.

Theoretically, a wound heals by reversion to the same process of growth that takes place embryologically. In dealing with tensile strength we are dealing with that type of growth which is represented by the mesenchyme. It goes through the same phases of multiplication of cells, and the most important phase, of course, is the multiplication of fibroblasts, because that is the basic underlying cell for all the structures which later have to do with tensile strength or with the supporting strength as in bone.

The early phase of that is, I think, perfectly clear; that is the phase we speak of as the fibroblastic in the healing of wounds. There has always been some difficulty in following from that phase through to the growth of specific tissues. That, perhaps, is most outspoken in the matter of production of bone or the healing of fractures, and there arises there always the question, which is not perhaps a very important one but, theoretically, is of considerable interest, as to whether the new tissue, such as bone, is reproduced from specific bone cells or whether it is reproduced from fundamental, underlying fibroblastic cells by a process of differentiation. I, myself, am pretty well convinced the latter is the case—that again, as in the embryo, these cells, governed by a somewhat mystical concept, perhaps that of the organizer, which is specific for the particular situation in which the cell is involved, go on to differentiate into specific tissues as they did originally.

While that may seem to have not much bearing on this paper, I think it has a great deal. We have all been familiar for a long time with the so-called Wolff's law, which is supposed to represent the adaptation of tissues to specific functions because of the functional activity of the tissue itself. That has been a rather vague concept, difficult to prove but fairly apparent in experience, I think. Now more recently I think there is some indication as to how that takes place. Of course, we have known for a long time that the hammering of iron will convert it into a wrought iron which has a quite different tensile characteristic, or the tempering of iron will convert it into steel which again has a quite different characteristic. Very recently, of course, it has been found that with the production of synthetic textile materials, one of the steps in the process is the stretching out of the textile thread which produces —and that is definitely known—a molecular realignment which is along the line of the stress imposed upon the thread. Thas was rather graphically stated many years ago by Sir Arbuthnot Lane, as the alignment of tissues along the lines of force.

That has a direct application and is illustrated here, I think, in Doctor Mason's work, by the fact which he has clearly demonstrated that at the stage where the cells have reached a fairly mature situation but have not become realigned along the lines of force, the introduction of active functional pull upon the tissues accelerates such realignment, and in effect is an essential point in the eventual development of the tendon with the functions of a tendon.

Practically speaking, I think this is very important. He has laid down now, I think, for the first time, with a great deal of certainty, the period that immobilization should be carried out in tendon healing, which is ap-

proximately that of two weeks; that a period then ensues where the strengthening of the tendon will occur more rapidly if there is a limited mobilization, and after a week or so a period when freer mobilization and greater strength can be thrown upon the tendon, not only without danger but with very definite benefit.

I also should like to point out that he has contributed something to the old question of how one shall suture a tendon. It is obvious that the important thing in the suture of a tendon is not primarily the suture material but rather the way the suture material is applied. The holding power of the suture, as everywhere else, is the important thing, and the corollary of that is that one should use a suture of just sufficient size and strength to meet that holding power. There is no importance in using a suture larger than that because it will tear out of the tissues, and there is a great deal of importance in using the minimum suture material that is necessary because the less you use the less disturbance there will be in the healing process. Interpreted practically, to my mind that means the use of a fine, nonabsorbable material, such as silk, which will retain its strength well beyond the period when you wish to start active mobilization of the tendon.

Dr. J. Albert Key (St. Louis, Mo.): I have nothing but commendation for the work. They showed beautifully the strength of the tendon healing at various intervals. Clinically, however, the thing that worries me when I suture tendons is not pulling out or breaking so much as their sticking, and that is what happens to a lot of mine. They form adhesions. I know that this is beyond the scope of this paper. However, there must have been some observations. From the lantern slides it seems to me that the tendons which were immobilized did not form as many adhesions as those which were moved. The reason we have moved our tendons early was to prevent adhesions. I wonder if something will not be said along that line in closing the discussion.

Dr. Summer L. Koch (Chicago, Ill.): I am sure you will agree that Doctor Mason and Doctor Allen have made a definite contribution in helping us to know how to direct, wisely, the postoperative care of the patient who has had a division and repair of tendons. If we were to ask our youngest surgical intern the principles of treatment of a fracture he would tell us very promptly that they are: First, reduction; second, immobilization; and, third, immobilization in such a position that there is no tension on the fractured fragments; in other words, in a position of physiologic rest. That the same principles apply to the treatment of ruptured tendons, nerves, and soft tissues is sometimes forgotten. The experimental studies that have been reported help us to understand the importance of applying these surgical principles in the treatment of ruptured tendons, and how it can be accomplished.

There is a second analogy, as Doctor Harvey has pointed out, between healing tendon and healing bone, in that function plays so important a part in the process. John Hunter, many years ago, quoted the importance of function in the repair of fractured bones and in determining the direction of the lines of stress; Doctor Mason's experimental work has indicated clearly how and when functional activity can be used advantageously in securing sound healing with a minimum of reaction about the site of tendon callus. As Doctor Key said, our attention has been focused on preventing the "sticking" of sutured tendons. The principles that apply to the healing of every type of "fractured" tissue have often been ignored.

DR. MICHAEL L. MASON (Chicago, Ill., closing): I appreciate Doctor Harvey's and Doctor Koch's discussions more than I can say. I was glad to have Doctor Key bring up the question as to the time for starting motion following tendon repair. Motion is started early because the surgeon wishes to prevent adhesions; however, the opposite is the case. I had hoped to make it a little clearer in my talk that early motion and, certainly, early active, unrestricted motion leads to the production of marked reaction and adhesions. In those tendons which have been kept absolutely immobile, however, we have the most perfect type of healing.

It is my feeling that restricted motion can be safely started at the end of about two weeks; that is, toward the end of the period of fibroplasia. Restricted use, with a splint which prevents overstretching of the healing tendon, allows us to take advantage of the functional stimulus without the danger of leading to reaction and producing binding adhesions.

PARTIAL MYOTOMY IN THE TREATMENT OF DIVIDED FLEXOR TENDONS OF THE HAND

A REPORT OF TWO CASES

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ONE of the few surgical conditions characterized by a marked disparity between morbidity and mortality is that of the divided flexor tendon. The poor functional results attendant upon this injury, and the technical care necessary for its proper treatment, have been repeatedly described.[1, 2, 3, 4] It is the consensus of opinion that normal function is lost in a considerable percentage of cases. Furthermore, the degree of crippling of the hand increases, the more radial the site of trauma.

The clinical contrast between flexor and extensor tendon injuries, especially in the presence of infection, has been explained in terms of the tendon sheath. It has been assumed that the uniformly good results following repair of the extensor tendons are referable to the diffuse blood supply and the absence of fragile tendon sheaths, which form adhesions on slight provocation.

There is a third factor of real importance which has heretofore, in my opinion, not been adequately treated, *i.e.*, tension at the suture line.

It is the surgical custom to apply a molded plaster splint following the operative procedure. The position of hyperextension is used in extensor tendon cases, and acute flexion where flexor tendons have been repaired. While this rests the muscle and decreases its tension, it far from obviates the pull at the suture site. This fact is amply demonstrated by the very real tension invariably found as divided flexor tendon ends are being approximated with the patient under complete anesthesia. Despite the immobilizing plaster splint, normal muscle tone exerts its continuous dehiscent force on the suture line during the entire postoperative period. This is considerably more marked with flexors than with extensors because of the preponderant muscle bulk of the former, normally expressed by a flexed attitude of the relaxed hand.

Following an unsuccessful outcome in a flexor tendon case, in which the suture line parted on the seventh day due, quite evidently, to the extreme tension at the site of repair, the possibility of relieving the muscle strain by partial myotomy was first considered.

From the viewpoint of function, the tendon is merely a cord transmitting the muscle pull. The reaction of muscle to injury such as laceration differs markedly from that of tendon. The former has a rich blood supply, healing promptly with minimal loss of strength. The highly contracted scar in a muscle belly does not seem to interfere with its subsequent function, a demon-

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strable fact in any extensive lacerated wound of the extremities. This is also characteristic of the smooth muscle sphincters, which heal rapidly following complete division.

The flexor muscles of the forearm are of the unipennate type with the tendon prolonged throughout the length of the muscle. Hence, division of the muscle which includes the tendon prolongation results in a loss of contractile power, the degree of which bears a direct relationship to the site of division. Since this point in the two cases herein described was selected at the junction of the distal third with the proximal two-thirds of the muscle, it is apparent that only those fascicles in the distal third were able to exert any pull through the tendon. As the muscle wound healed, uniting the divided portions of the muscle and the divided ends of the tendon prolongation, the muscle power returned so that, as in the first case, the patient regained more than two-thirds of the muscle strength within nine weeks of the time of operation. The myotomy wound evidently healed *pari passu* with the repaired tendon so that, during the second month of convalescence, the muscle power rapidly returned at a time when the tendon was once again able to bear the full stress.

There are two additional advantages to this procedure: First, following the myotomy, the interval between the divided tendon ends is diminished by an actual transposition of the tendon due to the gaping of the muscle wound. This amounts to at least one-half inch, serving to allow approximation of the tendon ends in addition to the main purpose of relieving the tension on them This may be of use in secondary tendon surgery as a substitute procedure for short, free tendon grafts. Second, following the procedure it is possible to place the hand and finger in a neutral or slightly flexed position. This is of real advantage during the period of convalescence since it is far easier to regain normal function in a finger so placed than in one that has been coiled up in the most acute flexion for a month postoperatively.

CASE REPORTS

Case 1.—Hosp. No. 33783; J. P., white, male, age 41, accountant, was admitted, April 18, 1939, shortly after a porcelain faucet handle crumbled in his right hand. Examination revealed an irregular transverse laceration of the center of the palm with complete loss of flexion of the interphalangeal joints of the index finger. There was also anesthesia of the radial half of the palm and of the opposing surfaces of the index and middle fingers. Operation was immediately performed, complete hemostasis being obtained by the use of a blood pressure cuff applied to the arm. The sublimis and profundus tendons to the right index finger were found to be completely divided. By extension of the wound it was possible to seize the divided profundus tendon ends. They were approximated under considerable tension. For that reason, with clean instruments, an incision was made in the lower third of the forearm through which the corresponding pofundus muscle belly was identified and isolated. At the junction of the distal and middle thirds of the muscle a short transverse incision was made resulting in almost complete relief of the tension at the site of injury so that the divided tendon ends, after the clamps holding them were cut away, were easily approximated with fine Pagenstecher linen thread using the Connell technic. The hand and finger were placed in 10° flexion and a dorsal plaster splint was maintained postoperatively for 25 days (Fig. 1). During this time guided active motion was allowed each day except on the tenth day

when, due apparently to edema, no motion was possible. The wounds remained clean. From the fourth week on, radiant heat, massage and active motion were instituted. The patient returned to work at the end of the fifth week. By the end of the seventh week there was a normal range of flexion and extension at the interphalangeal joints, with slight restriction at the metacarpophalangeal joints. By the end of the eighth week he could touch the tip of the finger to the palm. By the twelfth week the finger could be actively coiled up and moved in all directions with agility equal to that of the normal side (Fig. 2). As was expected, there was definite improvement in sensation, the prognosis remaining good for this aspect of the case. The patient was discharged with a normally functioning finger in the fifteenth week.

FIG. 1.—Case 1: The relaxed hand three weeks after injury. The flaccid index finger is lying in a neutral position with evident diminution of flexor tone.

FIG. 2.—Case 1: The relaxed hand 11 weeks after injury. The increased flexor tone of the index finger can be readily seen. The flexion of the other fingers is slightly increased, due to use of the hand.

Return of muscle power was tested by holding the forearm and finger rigid against a wooden splint and flexing the distal interphalangeal joint over the edge of the splint. At the end of the sixth week a four-pound weight could be easily moved over a pulley by the terminal phalanx throughout the full arc of flexion. By the twelfth week an eight-pound weight was easily so moved; by the fourteenth week, nine pounds. Control for the terminal phalanx of the normal index finger was 11 lbs. flexion.

Case 2.—Hosp. no. 34090: P. C., white, male, age 44, office-worker, was admitted, June 13, 1939, shortly after having broken a water bottle in his left hand. He suffered jagged lacerations of the ring and little fingers. There was no loss of sensation but there was complete loss of flexion of the interphalangeal joints of the little finger. At operation, only the divided profundus tendon ends were seized and brought together at the middle phalanx. As is characteristic of this finger, there was a good deal of tension. For this reason, an incision was made in the forearm just lateral to the ulnar vessels and nerves.

The flexor profundus digiti quinti muscle belly was readily identified. About half of the thickness of the muscle was divided, resulting in a definite diminution of tension with much easier approximation of the divided tendon ends. The myotomy wound gaped more than half an inch. The tendon ends were repaired with a fine linen, Connell suture. A posterior molded plaster splint was applied with the hand and finger in slight flexion. This was maintained for four weeks. During the second and third weeks there was a loss of the undercut skin overlying the suture site. The mucopurulent discharge from this point was evidently due to sloughing skin and not to a real infection. During the fifth week, there were a few degrees of flexion of the terminal phalanx and about 10° of the proximal interphalangeal joints. By the end of the sixth week the wound was healed. Physiotherapy has been administered since then.

SUMMARY.—One of the adverse factors responsible for the poor results attendant upon division of the flexor tendon is that of tension at the site of repair.

A simple method of myotomy consisting of simultaneous division of the tendon prolongation at a selected site in the forearm is proposed as a corrective procedure.

Evidence is offered that a muscle wound heals *pari passu* with the tendon, leaving no defect.

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DISLOCATION OF THE FIRST CERVICAL VERTEBRA*

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AND

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Classification.—Dislocation of the first cervical vertebra is the partial or complete loss of contact of the inferior articulating surfaces of one or both lateral masses of the axis with the corresponding superior articular facets of the epistropheus. The dislocation may be anterior, right or left rotary, posterior and right or left lateral. A fracture of the odontoid generally accompanies the latter two types.

Etiology.—The dislocation may result from trauma, infection, paralysis, or congenital defect. Automobile accidents, falls on stairs, falls from bed, sudden turns of the head, and postoperative overcorrection of torticollis are some associated causes. Traumatic dislocations are frequently associated with a fractured odontoid. The tip of the odontoid is securely attached to the basilar process of the occiput by the alar and apical ligaments. A force directed from the head is transmitted through these ligaments against the anterior arc of the atlas or the transverse ligaments as a fulcrum to be levered at the base of the odontoid. If the transverse ligament withstands the strain, the base of the odontoid is fractured.

Following infection, the ligaments supporting the atlas on the epistropheus become relaxed, permitting a spontaneous dislocation. The relaxation of ligamentous support may be due to bone destruction, bone decalcification or joint involvement. The vertebral bone may be destroyed by pyogenic, tuberculous or syphilitic osteomyelitis. Bone decalcification and joint involvement follow an adjacent cervical infection as sinusitis, pharyngitis, tonsillitis, mastoiditis, adenitis or dental abscess. The otolaryngologic literature classifies such a spontaneous dislocation following cervical infection as "Grisel's disease." Leriche and Poligard[5] explain the decalcification on the basis of calcium absorption from the hyperemia induced by the infection. Watson Jones[4] supports this in reporting a boy of nine years with a mastoiditis and cervical adenitis with a dislocation in which the roentgenograms revealed complete decalcification of the anterior arch of the atlas. Following reduction, and as the infection subsided, recalcification occurred. The joint involvement with distention of the capsule and stretching of supporting ligaments, Wittek and Jacobs[12] claim, is from the regional hyperemia. Coutts[2] believes the axoid-epistropheal joints are involved by direct extension of the infection through the lymphatics. The detachment of ligaments accompanying

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decalcification or stretching of the ligaments from joint involvement results in articular relaxation that permits dislocation. This may be gradual, from the position of comfort assumed by the head during the infection, or sudden, from an attempt to change the position of the head. The former is illustrated by Grieg[3] in citing a case reported by Benjamin Bell, 100 years ago, in which a dislocation of the atlas was recognized in a subject with a chronic pharyngeal ulcer. Sudden dislocation is noted by Watson Jones in a case with tuberculous cervical adenitis with sinuses. As the nurse attempted to change the position of the head to facilitate dressing, the subject died. The autopsy revealed that the first cervical vertebra had been dislocated with impingement of the spinal cord.

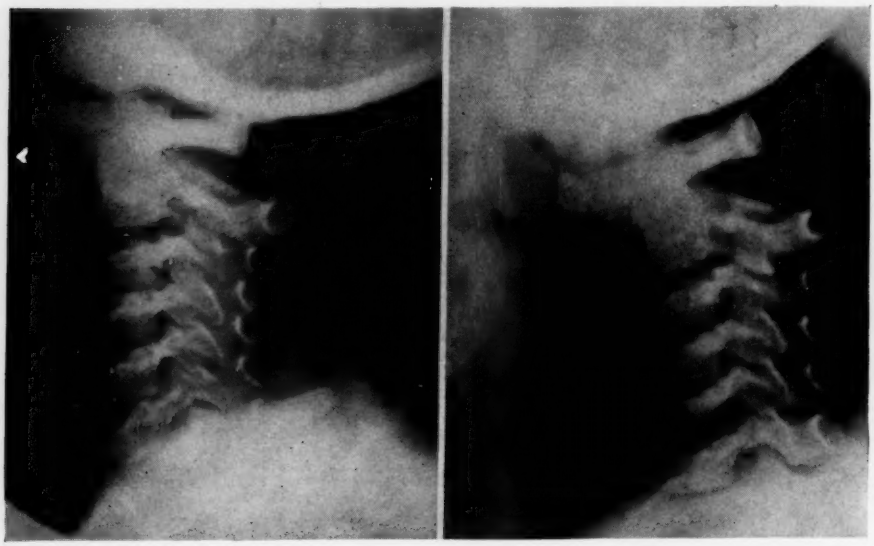
Paralytic dislocations from muscle imbalance have been accredited by Coutts as occurring in the subacute stage of poliomyelitis.

Congenital absence of the odontoid was reported by Roberts[10] as a cause for dislocation of the first cervical vertebra. This subject was a man, age 20, who was pivoting on his head in a gymnasium when something snapped at the base of his skull. He had sudden severe pain in his neck. Roentgenograms showed a forward dislocation of the first cervical vertebra and an absence of odontoid. The dislocation was reduced by head traction. Operative fixation was advised but refused. A leather collar was applied. The subject had no recurrences for one year but subsequently could not be located.

Anatomy.—The axoid-epistropheal relation is dependent upon three common articulating surfaces. The axis is constructed of two lateral masses joined anteriorly by a narrow mass of bone, the arcus anterior, and posteriorly by a similar but larger mass, the arcus posterior. The lateral masses articulate superiorly with the condyles of the occiput and inferiorly with the superior articulating facets of the epistropheus. The superior articulations are slightly concave to permit a rocking action. The inferior are almost flat to permit a gliding rotary action. Both superior and inferior articulations are in the horizontal plane. The inferior facets are, therefore, particularly dependent upon ligaments for support. The arcus anterior articulates with the odontoid process or dens of the second vertebra. The odontoid is a superior projection of the body of the second cervical vertebra. It has a flattened surface covered with cartilage both anteriorly and posteriorly. Across its posterior surface is stretched the transverse ligament from the two lateral masses of the atlas. From the tip of the odontoid extend two alar ligaments and an apical ligament to the occiput of the skull. These ligaments are covered by the tectoria membrane which extends downward from the basilar process of the occipital bone over the posterior surfaces of the vertebral bodies. The tectoria membrane, in turn, is covered by the posterior longitudinal ligament which has similar attachments. Anteriorly, the atlas is supported by the anterior longitudinal ligament which extends from the inferior surface of the basilar process of the occiput attaching along the anterior surface of the vertebral bodies. The posterior arch is bound to the posterior margins of

the foramen magnum by the atlanto-occipital membrane and the arch of the second cervical vertebra by the ligamentum flavum.

Diagnosis.—Coutts gives an excellent description of the interpretation of clinical and roentgenologic diagnosis of axoid-epistropheal dislocation. The authors agree that the diagnosis is indicated by few constant symptoms and signs, and that the verification of the diagnosis is determined by the roentgenogram. The head is held in a torticollis position. The chin is frequently held tightly against the larynx. It is often difficult to open the mouth. Dysphagia and voice change may be observed. Pain is in the occipital and mastoid areas due to pain reference in the distribution of the second cervical nerve. These areas are tender to touch. Motion, particularly extension, increases the pain.



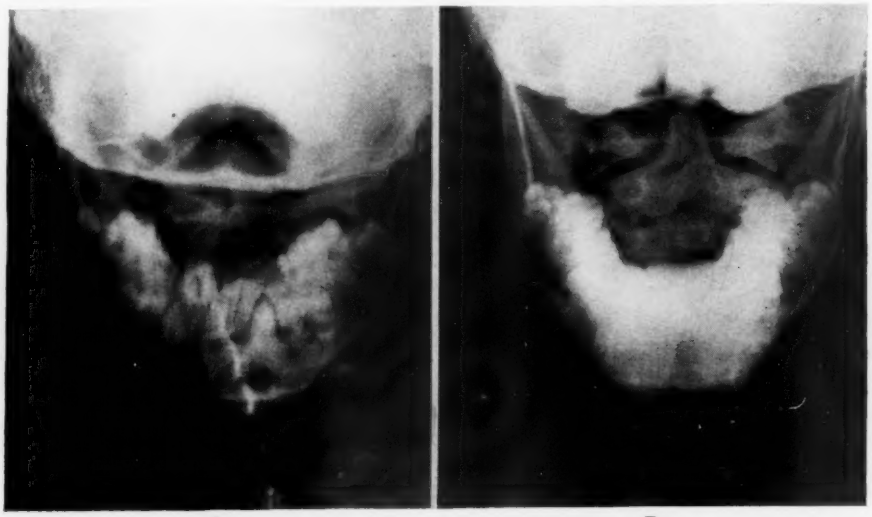
A. B.

FIG. 1.—Case 6: Lateral view of cervical spine showing anterior dislocation of the first cervical vertebra. A. Shows the spine is in maximum extension. B. Shows the spine is in maximum flexion. These comparative films show the extent to which deformity is exaggerated in the flexed position. This is of value in the follow-up examination to clarify the question of luxation, after the plaster case immobilization, applied after reduction has been removed.

The subject rises, supporting the chin in his hands. On attempted cervical motion, grating of the neck is experienced. This may be audible to the examiner. The head can be laterally flexed but slightly from the side to which it is tilted. The chin cannot be rotated past midline in attempting to correct the rotation deformity so that the subject must turn his entire body to see over the opposite shoulder. Posteriorly, the paraspinal muscles are prominent on the side to which the chin rotates. This prominence is accentuated if any attempt is made to straighten the head. If the mouth can be opened, the pharynx will bulge on the side to which the head is tilted. Paralysis is relatively infrequent in those cases surviving the force producing the dislocation. When present, however, it is more common in the arms. Sensation may be retained as the pyramidal decussation lies directly behind the odontoid. Death may be im-

mediate if the medulla is compressed, but the diameter of the foramen magnum permits considerable displacement without cord compression.

The roentgenologic diagnosis is dependent upon anteroposterior and lateral views. If the lateral views are taken in maximum extension and maximum flexion of the cervical spine, the dislocation is found exaggerated by flexion (Fig. 1 A and B). There is a lordosis of the lower cervical spine. The anterior arch of the atlas appears more than 2 Mm. anterior to the odontoid, unless the latter is fractured. The posterior arch of the atlas appears broader in unilateral dislocations as it is tilted. If lines are drawn through the inferior



A. B.

FIG. 2.—Case 5: A. Shows a left rotary dislocation of the first cervical vertebra. A typical torticollis position of the head is shown. The overlap of the lateral masses of the atlas and their asymmetrical relationship to the odontoid is visualized. B. The same, following reduction.

surface of the first cervical and the base of spine of the second they will be found to converge rather than parallel one another. The odontoid, if fractured, fails to appear as a continuation of the body of the second cervical.

The anteroposterior view is difficult to obtain as the head frequently cannot be extended nor the mouth opened (Fig. 2 A and B). The second cervical spine appears as an inverted V and is deviated to the side to which the chin is rotated. The successive cervical spinous processes gradually return to midline. Accompanying the rotation deformity, a widening of one and a narrowing of the other lateral facet between the first and second vertebrae or loss of space between both facets is observed. When the odontoid is fractured it may appear nearer to one lateral mass than the other.

The vertex-mental view is advocated by Pendergrass and Chamberlain[9] as an aid in the roentgenologic diagnosis of dislocation of the first cervical vertebra. They state that this is taken diagrammatically opposite from the view described by Hirtz (Fig. 3). The anterior arch of the atlas projects away from the odontoid process. One lateral mass of the atlas is more closely ap-

proximated to the odontoid. This lateral mass fails to superimpose with the superior facets of the epistropheus. A transverse process and the spinous process of the epistropheus both project from either half of the posterior arch of the atlas.

Differential Diagnosis.—The diagnosis of dislocation of the first cervical vertebra is readily confused in the absence of a traumatic injury. Brookes[1] cites that children are frequently irritable during the prodromal stage of an infection and may be subjected to some form of punishment as a shaking or spanking which, though unrecognized at the time, exerts sufficient trauma to initiate the dislocation. Padula and Tracey[8] recently reported such a case in a four and one-half-months-old infant, who developed respiratory difficulty

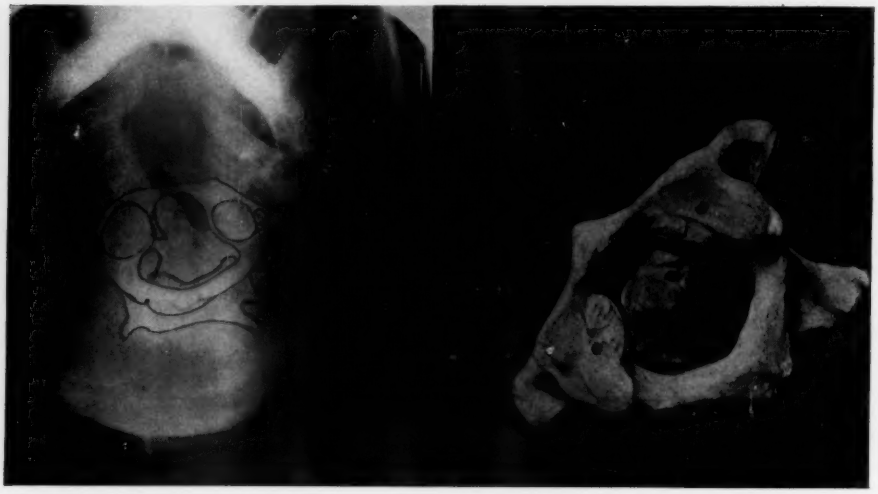


FIG. 3.—Case 5: A vertex-mental view of a left rotary dislocation of the atlas showing a retouched roentgenogram, and corresponding dislocation in an anatomic specimen.

following a shaking by an irate father because he was annoyed by its cries. Generally the torticollis deformity is not recognized until after the illness. Woltman and Meyerding[13] suggested that the absence of neurologic findings could account for mistaken diagnoses of pharyngeal abscess and cervical arthritis; while less frequently the delayed and gradual onset of neurologic symptoms would be confused with cerebellar tumor, syringomelia, bulbar palsy and myasthenia gravis.

Treatment.—The dislocation should be reduced as soon as possible after recognition. A method has been employed[7] by which the weight of the dependent head results in spontaneous reduction. This method is not adaptable for posterior dislocations of the first cervical vertebra which are accompanied with a fractured odontoid, as, theoretically, the deformity would be increased and cord compression could result. Caution is indicated in its immediate application after traumatic dislocation in which edema of the cord would cause a further paralysis. In treating fracture dislocations in other regions

of the cervical spine by this method it was learned that children tolerated it better than adults. An uncomfortable complication in adults was edema of the scalp.

Method.—Two or three short mattresses are placed on the fracture bed (Fig. 4). The head is gradually, for the first 24 to 48 hours, extended further over the end of the top mattress until the subject's shoulders rest on the edge of the mattress. The head then hangs free for another 24 to 48 hours. The subject is held in position by applying Buck's extension to the legs and raising the head of the bed. When rotation and lateral flexion of the head are free and equal in both directions, reduction has been accomplished. The reduction is checked roentgenologically simply by transferring mattresses and child with head hanging over the end onto a stretcher and transporting him to the

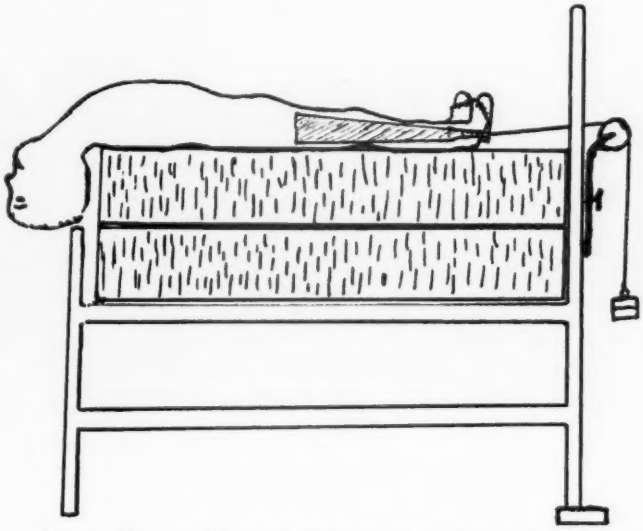


FIG. 4.—Diagrammatic representation of the position of the patient in bed, which is employed in the treatment of a dislocation of the first cervical vertebra.

roentgenologic department, if no portable apparatus is available. Roentgenograms are taken without disturbing the position of the head by holding a casette on the side of the neck for the lateral view and repeated with the casette in back of the head for the anteroposterior view.

Reduction is maintained by a plaster bandage from head to pelvis. It is necessary to have the chin and forehead included so as to prevent flexion of the head, which would cause redislocation. The plaster encasement is extended to the pelvis so that its weight is borne more comfortably by the patient. The method of applying the plaster bandage is to transfer the patient from the mattress without supporting the head, so that his back rests on the canvas sling of an Abbott frame and the head hangs dependent. A body jacket is then applied. As this dries, a table of suitable height is pushed beneath the patient. The canvas sling is released so that the table supports the patient's trunk. The Abbott frame and sling of canvas are then removed.

A four-inch muslin bandage, with a longitudinal slit in its midportion which will permit it to be slipped over the patient's head to run beneath the chin and occiput, is arranged so that the ends may be tied behind the operator's back. In this way the operator can exert traction and control the amount of extension of the neck. The extension which occurs at the occipito-axoid joint is not necessary, and not desired, as it will fix the subject's head looking heavenward. The head encasement is then applied over the traction bandage, which can be withdrawn after the head and body parts of the plaster case are joined together.

The fractures of the odontoid were held for 12 weeks in plaster, and then a Thomas collar worn for eight weeks.

The dislocations were held for 16 weeks in plaster, and four to eight weeks with a Thomas collar. The Thomas collar was necessary in order to permit rehabilitation of the cervical muscles. The atrophied muscles readily fatigued, thus permitting strain on the ligamentous structures. The strain caused pain and could produce another dislocation. The motion of the cervical spine permitted by the Thomas collar allowed the musculature to develop without the hazard of fatigue and ligament strain.

CASE REPORTS

Case 1.—T. S., male, age 7½, on March 3, 1935, was in a tussle, in which another boy had him in a head-lock. He had pain in the occipital region. The head was held tilted to left and rotated to right. He was admitted to the Graduate Hospital the same day. Roentgenologic examination revealed a fracture of the odontoid base with posterior displacement of one-quarter the breadth of the base. Traction was applied to the head by means of a Sayre collar and a four pound weight. The neck was held in slight extension by means of a partially inflated air-ring beneath the shoulders. After reduction was verified roentgenologically, a plaster encasement was applied from head to pelvis. This was worn three months, after which a celluloid Thomas collar was applied and worn for three months. Roentgenograms taken one year later (March 23, 1936) showed a very slight anterior position of the odontoid and obliteration of the fracture line. There was full motion in the cervical spine, and no deviation of the head.

Case 2.—M. D., colored, female, age 3½, had her neck stepped on by an adult, 48 hours before admission to the Children's Hospital, August 25, 1936. She complained of pain in neck and would not turn her head. The head was tilted to the left and the chin was rotated to the right. Roentgenograms showed a fracture at the base of the odontoid, with anterior displacement (Fig. 5 A and B). After 48 hours of dependent head traction, a plaster encasement was applied from the head to the pelvis. This was worn three months. A Thomas collar was then worn for two months. At examination May 24, 1937, there was but slight deviation of the head and full range of cervical spine motion. Roentgenograms showed the fracture healed and the dislocation reduced.

Case 3.—J. D., male, age 60, had delirium tremens and fell downstairs May 30, 1935, sustaining a fracture of the odontoid, with anterior displacement of the first cervical vertebra, and a fracture of the right humerus. He was admitted the same day to the Philadelphia General Hospital. He had no neurologic involvement. Due to mental confusion, it was necessary to feed him through a nasal tube. He developed a decubitus ulcer on his chin from the Sayre collar traction. The dependent weight of the head was tried. In 24 hours, reduction had been accomplished. A plaster encasement was applied from head to pelvis. The patient tore off the encasement 24 hours later. He was transferred to the psychiatric ward. The reduction could not be maintained with

Sayre traction. No symptoms referable to cord pressure developed up until his death six weeks later from pneumonia.

Case 4.—W. S., colored, male, age ten, was admitted to the Children's Hospital November 16, 1936. Three weeks before admission, during illness from acute tonsillitis, he awakened one morning with pain in mastoid region and a stiff neck, which forced him to hold his head tilted to right and the chin rotated to left.

Roentgenologic examination revealed a forward dislocation of the right lateral mass of the first cervical vertebra. He was treated with his head hanging dependent as described. After four days, the roentgenogram verified the reduction and a plaster jacket from head to pelvis was applied. After four months (March 25, 1937) the encasement was removed and a Thomas collar applied, which was worn for one month. On examination March 14, 1938, there was a questionable tilt of head to the right.

A. B.

FIG. 5.—Case 2: A. A fracture through the base of the odontoid, with anterior dislocation. B. The same, three months after reduction.

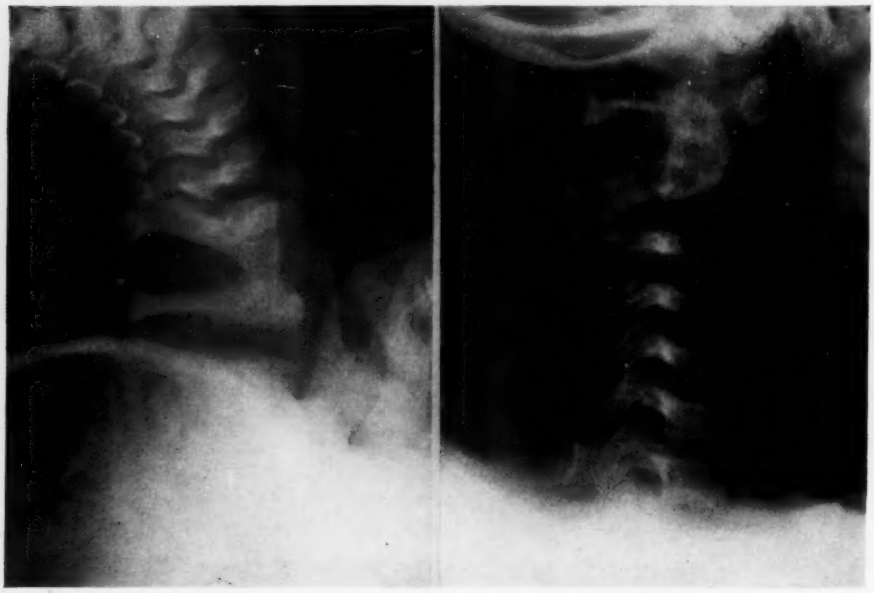
Lateral flexion of the cervical spine was 20° less to the left than to the right. Other motions were unimpaired.

Case 5.—B. T., female, age eight, had a prolonged history of upper respiratory infection and pharyngitis. She had had cervical adenitis for five weeks. For two weeks prior to admission to the Mary Drexel Home May 9, 1938, her head had been turned with the chin on the right shoulder and head tilted anteriorly. Examination revealed the head held in 70° rotation to the right and 30° flexion to the left. Rotation of the head to the left could not bring the chin within 30° of the midline. Rotation of the head to the right was 100°. Flexion to left was 45°. Flexion to the right was zero. No other physical signs were present. Roentgenograms showed a rotary displacement of the atlas to the right, with a luxation of the occipital condyles to the right on the lateral masses (Figs. 2 and 3). With the head hanging dependent the dislocation reduced in 48 hours. The usual type of plaster encasement was applied and worn for three months, after which a leather-reenforced collar was worn for two months. At

examination December 2, 1938, the roentgenogram showed reduction maintained. The chin was, clinically, slightly to right of the midline but the cervical motions were equal.

Case 6.—D. S., female, age three, was admitted to the Children's Hospital June 2, 1936. She had had measles six weeks previously which was followed by a cervical adenitis and bilateral otitis media. The neck had been held stiffly with the head turned to the right for a week. There was anterior displacement of both lateral masses (Fig. 1). Head traction by means of a Sayre collar was tried in this case for four weeks without success. Reduction occurred in 24 hours when the head was allowed to hang dependent (Fig. 6A and B). A plaster encasement was applied from head to pelvis. This was changed at the end of three months and removed in four months. A Thomas collar was worn six weeks.

January 4, 1937, two weeks after removal of Thomas collar, dislocation recurred.



A. B.

FIG. 6.—Case 6: A. Showing reduction with head hanging dependent. Note the amount of distraction between the occiput and first cervical vertebra, denoting ligamentous relaxation. Lateral films prior to reduction are shown in Figure 1. B. Following surgical fixation, in which the laminae were wired together.

Reduction was accomplished with the head dependent and a plaster encasement was applied on the third day. At end of five months the encasement was removed and a Thomas collar applied. One week after removal of Thomas collar the second time, a recurrence of dislocation was observed.

Operation.—July 29, 1937: An open reduction of the first and second cervical dislocation was performed through a posterior midline incision. The head of patient was held in position by means of a plaster bed. Traction on the posterior arch of the first cervical vertebra was made by a towel clip in order to approximate it to the arch of the second cervical vertebra. The arches were lashed together, as advocated by Osgood and Mixter,[6] with a strip of fascia lata from the thigh. A jacket was worn four weeks and a Thomas collar applied. The dislocation again recurred. *Second Operation.*—August 2, 1937, the fascial suture was found to have pulled free from its silk sutures. It was then observed that a mistake had been made in not knotting the fascia to itself and securing the knot with silk. This time, two wire sutures were passed around the posterior arches of the first and second cervical vertebrae, and an attempt was made to

obtain bony fusion between them by removing the ligaments and cartilaginous covering and overlapping pedicle grafts.

Four months later the plaster encasement was removed. The position had been maintained and a Thomas collar was applied and worn three additional months.

At examination June 1, 1939, 21 months after the second operation, the head was held with a slight tilt to the left. Extension 30°. Flexion 45°. Rotation 25° left, 45° right. Lateral flexion, bilateral, 45°. There were no neurologic findings. Roentgenograms showed no forward luxation with flexion, according to comparative lateral roentgenograms with the cervical spine in maximum extension and flexion.

TABLE I

SUMMARY OF SIX CASES OF DISLOCATION OF THE FIRST CERVICAL VERTEBRA

Case	Initials	Age	Etiology	Dislocation	Complication	Result
1.	T. S.	7½	Trauma	Posterior	Fracture odontoid	Reduced
2.	M. D.	3½	Trauma	Anterior	Fracture odontoid	Reduced
3.	J. D.	60	Trauma	Anterior	Fracture odontoid; fracture right humerus; delirium tremens	Death from pneumonia
4.	W. S.	10	Spontaneous. Ac. tonsillitis	Right. Rotatory	None	Reduced
5.	B. T.	8	Spontaneous. Cervical adenitis	Left. Rotatory	None	Reduced
6.	D. S.	3	Spontaneous. Measles. Cerv. adenitis. Bilateral otitis media	Anterior	Three recurrences. Two open fixations	Reduced

Discussion.—In the six cases reported, the traumatic and spontaneous dislocations were equally divided (Table I). The traumatic dislocations were associated with a fractured odontoid. One of this group had a posterior dislocation. There were three anterior dislocations, one spontaneous and two with a fractured odontoid. The two remaining spontaneous dislocations were rotatory. The spontaneous dislocations had been preceded by a regional cervical infection and not by an involvement of the vertebra. No neurologic symptoms were encountered in this group.

With the exception of the posterior dislocation, all reduced spontaneously by permitting the head to hang dependent.

The reductions were maintained by a plaster of paris bandage from forehead including the pelvis. The fractured odontoids were held three months. The spontaneous dislocations were immobilized for four months. After the removal of the plaster bandage, a Thomas collar was used on an average of six weeks, until the cervical muscles were rehabilitated. At the end of six months, if lateral roentgenograms, taken with the head in maximum flexion, showed no luxation of the axis, the dislocation was considered reduced.

There were two complications in the series. The one, Case 3, a male, age 60, with delirium tremens in which fixation was abandoned, developed pneumonia six weeks subsequently and died. The other, Case 6, was a child who had three recurrences without attributable trauma; two, after two complete six-month fixation periods; the third, four weeks subsequent to operative fixation, in which fascia lata was used to fasten the laminae of the first and second cervical vertebrae together (Fig. 7). An error in the operative technic was found responsible for the third recurrence of the dislocation. The ends of the fascia lata suture were not knotted before being sewn together with silk, so that they pulled free.

SUMMARY.—Dislocations of the first cervical vertebra were a result of trauma, infection (spontaneous), muscle paralysis or congenital defect. The ligaments supporting the axis and epistropheus normally prevented luxation. A force, on the other hand, levered by the ligaments, resulted in a fracture of the odontoid. Six cases of dislocation of the first cervical vertebra, ranging from three to 60 years of age, are reported after observation from one to four years. Three cases had a traumatic history and were associated with a fractured odontoid. Three were spontaneous dislocations following associated

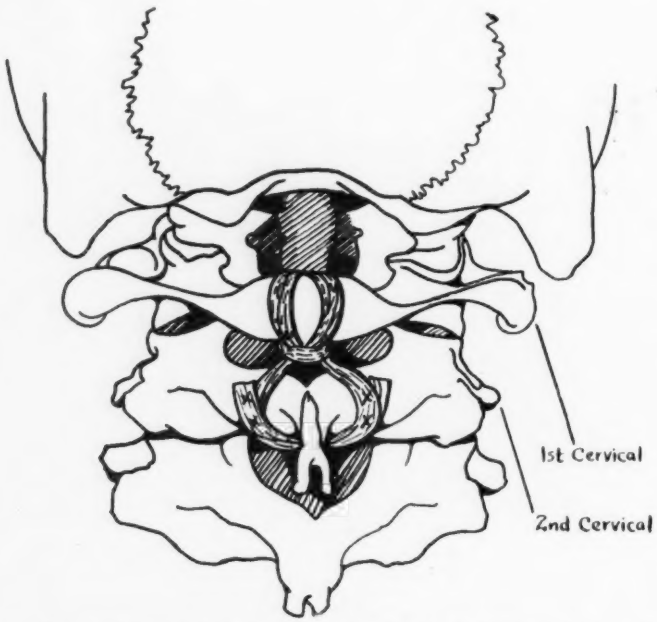


FIG. 7.—Drawing showing the technic employed for fastening the laminae of the first and second cervical vertebrae with fascia lata. (Modification of the method advocated by Mixter and Osgood.[6])

infections in the cervical region. One case with a fractured odontoid had a posterior dislocation. Two had anterior dislocations. One spontaneous dislocation had an anterior dislocation, two spontaneous dislocations had rotatory displacement, one to the left and the other to the right. No cases had any neurologic disturbance from the dislocation. All except the posterior dislocation were reduced spontaneously with the head hanging dependent. Reductions were maintained by a plaster of paris bandage, including forehead and pelvis, for three months if associated with a fractured odontoid, and four months if spontaneous. A Thomas collar was used for six additional weeks. There were two complications. One case, with delirium tremens, was uncooperative, reduction could not be maintained by plaster fixation and death resulted from pneumonia. The second case had three recurrences in 15 months, each time after mechanical fixation was discontinued. This patient had two surgical attempts made to maintain reduction. The second surgical

procedure has remained successful for 21 months, with no external fixation for 17 months.

CONCLUSIONS

(1) Dislocation of the first cervical vertebra is commonly caused by trauma or infection.

(2) Traumatic dislocations are frequently associated with a fractured odontoid.

(3) The infection is rarely in the vertebra but in the surrounding cervical tissues. The dislocation in such instances is spontaneous.

(4) Neurologic complications are infrequent. Those reported in the literature are immediate or delayed, and gradual in onset.

(5) Dislocations of the first cervical vertebra can be safely and easily reduced spontaneously with the head hanging dependent, except posterior dislocations or in the presence of neurologic complications.

(6) A recurrence of a dislocation after described care requires operative fixation.

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BRIEF COMMUNICATIONS AND CASE REPORTS

A MECHANICAL AID FOR VENIPUNCTURE

FRED F. RUDDER, M.D.
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THIS INSTRUMENT was designed to facilitate venipuncture where large-sized needles (No. 13 to 16 gauge) are employed in transfusions. The underlying principle has been evolved after an experience of approximately 1,000,000 venipunctures, over 60,000 of which have been performed by the author during the past two years.

FIG. 1.—Showing the mechanics of the device employed, and the method of its introduction into a vein.

It has been my experience that venipuncture can best be performed by fixing the vein with the thumb, and, with the bevel of the needle up, the skin is punctured over the vein. A backward pull is then made on the plunger of the syringe as the vein is being entered. When the lumen of the vein is entered, blood fills the syringe. The disadvantages of using an ordinary syringe are: (1) The barrel, even with an eccentric tip, prevents the needle from being inserted parallel to the long axis of the vein by striking the arm or thumb; and (2) pulling back on the plunger while entering the vein may be an awkward procedure.

The device, as illustrated in Figure 1, obviates the above objections, in that the handle is of sufficient length so that the needle may easily parallel the vein, and when the lumen of the vein is entered blood immediately flows out of the perforated passage. The handle fits snugly into the palm of the hand where even pressure can be exerted, affording perfect control over the tip of the needle at all times.

Submitted for publication November 25, 1939.

DELAYED HEMORRHAGE FOLLOWING TRAUMATIC RUPTURE OF THE SPLEEN—WITH PARTICULAR REFERENCE TO ROENTGENOLOGIC FINDINGS*

CASE REPORT

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TRAUMATIC RUPTURE of the spleen and its attendant hemorrhage has become recognized as a definite, though somewhat unusual, clinical entity. It is also recognized that considerable variations in symptoms occur and that these variations depend upon the severity of the splenic injury, the quantity of blood lost, and the rate of blood loss. The patient may become exsanguinated as rapidly as when an aortic aneurysm bursts. Or, after an initial injury, the patient may exhibit obscure abdominal signs over a period of days or weeks, and gradually go down hill until the presence of continued internal hemorrhage is recognized and treated. Usually the initial injury is followed by a so-called latent period of a few hours, followed by the symptoms and signs of internal hemorrhage. Much more rarely this latent period continues over a period of days or weeks, the patient goes about his business, and the primary injury is ignored or even forgotten. Bleeding has stopped. Then, under strain of a slight rise in blood pressure, profuse secondary hemorrhage sets in, the patient is prostrated, and prognosis is grave.

This syndrome of delayed hemorrhage following traumatic rupture of the spleen has been reported by various authors. In 1932, McIndoe[1] published a report of such a case, and in addition collected 45 cases from the literature.

In contrast to the usual case of splenic rupture where the injury is severe, cases of delayed hemorrhage from splenic rupture usually have a comparatively slight primary injury. Direct violence to the left lower thorax or left upper abdomen is the common trauma although a case of delayed hemorrhage has been reported where the patient was thrown to the ground, striking the right side of the abdomen. Frequently fractures of the lower left ribs are present.

Symptoms are few and may be limited to transient dizziness. Collapse, followed by rapid recovery, has been reported. Pain over the spleen is frequently present. There may be radiation of pain to the left shoulder. The abdominal signs may be limited to slight epigastric or left upper quadrant rigidity. And in some instances no signs have been present and the patient complained only of a little discomfort or a dull ache in the left side.

The latent period in these cases is usually three to nine days. Rarely, it may be 14 or more days, and in one case on record it lasted six months. During the latent period a diagnosis can sometimes be made by persistent pain, tenderness,

* Read before a joint meeting of the New York Surgical Society and The Philadelphia Academy of Surgery, Philadelphia, February 14, 1940. Submitted for publication December 22, 1940.

rigidity, or signs of splenic enlargement. When secondary hemorrhage takes place, it often occurs spontaneously. At other times a minor effort such as straining at stool or bending over is sufficient. Apparently very little stress is required to break down whatever protective barriers may form in and around the injured organ.

When secondary hemorrhage occurs, variations between cases diminish and a rather uniform symptom sequence is found. Sudden severe pain, abdominal tenderness and rigidity, and the signs of shock develop rapidly. Death may occur before anything can be done. In patients who do not die at once, the signs of fluid in the abdomen, and an elevated left diaphragm can usually be found. Frequently there is radiation of pain to the left shoulder.

The prognosis is grave; operation is imperative. The mortality is in the neighborhood of 27 per cent. At the time of operation the spleen is often found widely torn or even shattered into several pieces, findings which attest to the violence of the secondary hemorrhage.

The present citation is of special interest because of the roentgenologic findings. Films were made at the time of secondary splenic hemorrhage, and after recovery.

Case Report.—A male, age 24, was admitted to the Abington Memorial Hospital, in December, 1939, complaining of pain in the back, the left shoulder and the abdomen. He had been riding in an automobile which had overturned, and, allegedly, he was unconscious for a short time after the accident. Examination revealed a young man suffering moderate pain. Examination showed fracture of the nose, left clavicle, left scapula, and left third and fourth ribs. There was lower abdominal tenderness with moderate rebound tenderness referred to the right lower quadrant. Some left upper quadrant pain was noted. No rigidity was present, no masses were felt, and no fluid could be demonstrated. Temperature 98.2° F.; pulse 80; respirations 26. Blood pressure 114/80. Blood count: 91 per cent hemoglobin; R.B.C. 4,400,000; W.B.C. 13,800; 86 polys, 11 lymph, 3 monos. Urine normal.

During the first 48 hours in the hospital the patient had slight right lower quadrant pain, and at one time he complained of transient left upper quadrant pain. Thereafter he had no abdominal symptoms. Pain in the left shoulder region was a prominent symptom, but the clavicular and scapular fractures could well have accounted for it. Eight days after the accident the patient was discharged to the Fracture Clinic.

Twenty days after the accident he reported to the clinic. Slight pain was still present in the left clavicular and scapular regions. In retrospect, the pain in the shoulder region might have prompted a diagnosis of ruptured spleen with perisplenic hematoma, but there were no abdominal symptoms or signs, and the pain was no more than one would expect from his injuries to the shoulder girdle.

All went well until 23 days after the accident when, during coitus, the patient suddenly experienced agonizing left upper quadrant pain. The pain was sharp, continuous and prostrating in severity. It quickly spread to the midline and then to the entire abdomen but the point of maximum severity remained in the left upper quadrant. He was seen by his family physician who sent him to the hospital with the diagnosis of ruptured peptic ulcer. At this time examination showed a pale, apprehensive man in severe pain. The skin was cool, the pulse was thin, the respirations costal in type. Diffuse abdominal tenderness was found, and it was most marked in the left upper quadrant. There was no radiation of pain to either shoulder. Generalized rigidity was also present, and was most marked in the left upper quadrant. Shifting dulness was elicited. The general picture bore some resemblance to acute pancreatitis and to ruptured peptic ulcer.

Temperature 98.2° F.; pulse 108; respirations 21. Blood pressure 124/92. Blood

count: 85 per cent hemoglobin; R.B.C. 4,000,000; W.B.C. 23,300; 95 per cent polys, 3 lymph, 2 monos.

A roentgenogram of the abdomen revealed no free air but showed tenting and elevation of the left dome of the diaphragm (Fig. 1). This finding was the most important single sign which led to the correct diagnosis. A diagnosis of secondary hemorrhage from a ruptured spleen was made and the patient was operated upon shortly after readmission to the hospital.

At operation, the peritoneum was slate-colored, and when it was opened huge quantities of blood and blood clots were noted throughout the abdominal cavity. Puddling of blood had occurred in both lumbar regions and in the pelvis. The spleen was somewhat enlarged and it was quite adherent to the lateral parietal peritoneum. A large gaping rent was oozing blood from the anterior splenic surface. Splenectomy was performed.

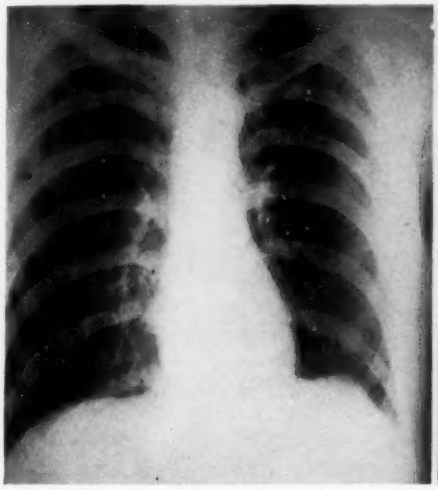

FIG. 1.—Preoperative roentgenogram showing tenting of left diaphragm.

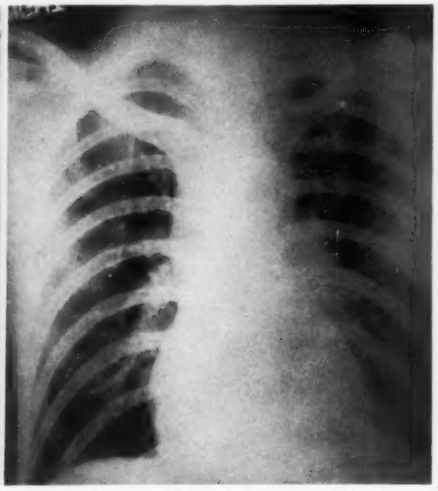

FIG. 2.—Postoperative roentgenogram showing a normal diaphragm.

After operation the patient was transfused on two occasions. His course was uneventful. A chest roentgenogram, taken before discharge, showed a normal diaphragm (Fig. 2).

In cases of delayed hemorrhage from the spleen the primary injury may be classified in three groups: (1) Minor superficial capsular rupture; (2) intrasplenic hematoma and subcapsular hemorrhage without capsular rupture; and (3) capsular and parenchymal rupture with perisplenic hematoma. In some cases the hematoma takes the form of a blood cyst. Tears of the hilum are usually followed by brisk and continuous hemorrhage. The case reported was one of capsular rupture with perisplenic hematoma.

This case illustrates a number of the characteristics of this syndrome as well as the difficulties in making a diagnosis before the final hemorrhage develops. The initial symptoms were quite characteristic. As often happens, signs were absent, and the symptoms were masked by other injuries. The latent period was somewhat longer than usual. When secondary rupture occurred, the specific signs of abdominal fluid and elevation of the left diaphragm, with tenting, were present in addition to the general signs of abdominal tenderness and rigidity, most marked in the left upper quadrant. There was no radiation of

pain to the left shoulder. The preoperative roentgenologic examination was particularly valuable in establishing the correct diagnosis. At operation, while the spleen was not actually fragmented, it was badly torn. Characteristic, were the presence of other injuries sustained at the time of primary splenic injury which masked the symptoms of primary splenic rupture.

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ERRATA

In the ANNALS OF SURGERY, **112**, page 741, in the bibliographic reference 10, the term "neurolemmoma" should have been spelled "neurilemoma," which is the word originally employed by the author of the article, Dr. A. P. Stout.

CORRECTION

Article by John Scudder, M.D.: Studies in Blood Preservation, ANNALS OF SURGERY. **112**:502–519, 1940, in Tables III, V and VI the last two items in headings below Composition should read ϕ/A and γ/A. The last two items below Mobilities, U x 10^{-5} should read ϕ γ.

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